

COVID-19 in pregnancy: A UK perspective

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Summary/Abstract

COVID-19 infection in pregnancy can cause respiratory and obstetric complications,¹ however emerging evidence on its impact in pregnancy is limited. This article aims to review data collected and analysed so far over the course of the coronavirus pandemic, that examine demographic associations, patterns of disease, severity and outcomes of COVID-19 in pregnancy in the UK.

Hospital admission, for which black and minority ethnic background and raised body mass index are risk factors, is associated with maternal mortality and admission to intensive care and is more likely in the late second or third trimester.² Vaccination is safe in pregnancy³ and is protective against severe COVID-19 and admission to intensive care.^{4,5} Maternal SARS CoV-2 is associated with a greater risk of stillbirth, preterm birth, small for gestational age (SGA) and preeclampsia.⁶ Efforts to reduce the incidence of COVID-19 in pregnancy, including vaccination, are therefore likely to reduce preventable complications from this disease.

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Introduction

SARS CoV-2 infection can affect many organ systems, but typically causes a range of respiratory presentations ranging in severity from cough and anosmia to pneumonia and respiratory failure requiring cardiorespiratory support.¹ From the beginning of the pandemic in 2020, little was known about how SARS CoV-2 infection behaved in pregnancy. Knowledge about other viruses, such as influenza⁷ and hepatitis E,⁸ which are associated with more severe disease in pregnant women, quickly made health care professionals concerned about the effect of SARS CoV-2 in pregnancy and demonstrated the urgent need for more information in this setting. Observational data were therefore collected in the UK, to aid understanding of demographic associations, maternal morbidity, mortality and neonatal outcomes of pregnant women who became infected. Initially, the number of pregnant women presenting to secondary care with COVID-19 in the UK was relatively small, however even in small numbers some important demographic patterns emerged from the data collected. Larger international studies also supported these findings. This article aims to summarise outcomes and patterns of disease in the UK with a focus on findings from the UK Obstetric Surveillance System (UKOSS) and the Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries in the UK (MBRRACE-UK) group.

Throughout this article, SARS CoV-2 will be used to describe the virus, and COVID-19 the clinical illness that results from SARS CoV-2 infection.

Review of current evidence – patterns of disease in the UK

Demographic data on women with COVID infection in pregnancy

Between 1st March 2020 and 14th April 2020, UKOSS collected prospective data on all symptomatic pregnant women who were hospitalised with COVID-19 in all obstetric units across the UK during that period (total 427).² The primary maternal outcome measure of this cohort study was the incidence of hospital admission, although maternal mortality, intensive care admission and fetal and neonatal outcomes were also examined.

The majority of pregnant women admitted were in the late second or third trimester, raising the likelihood that infection was more severe and respiratory support was more likely to be required with advanced gestation. The level of care required for respiratory support was noted and found that 10% of these women required intensive care admission with 1% undergoing extracorporeal membrane oxygenation (ECMO). Between 1st February 2021 and 30th September 2021, data collected by UKOSS revealed a further 1714 pregnant women were admitted with symptoms of COVID-19, and 14% (235) of these women were admitted to intensive care.⁵ Despite the RCOG recommendation for all eligible pregnant women to receive both doses of COVID vaccine⁹ and evidence to support vaccine safety,³ 98.1% of the women admitted had not been vaccinated, 1.5% had received a single dose and only 0.4% had received both doses. Furthermore, of the women admitted to intensive care during this period, 98.7% were unvaccinated and none had received both doses (Figure 1). Lower uptake of the COVID vaccine in pregnant women compared to the rest of the population has been reported and is concerning.¹⁰ These findings support the evidence that COVID vaccination in pregnancy reduces the likelihood of severe COVID-19, hospital admission and admission to intensive care.¹¹

The characteristics of the women demonstrate an association between hospital admission and black and other minority ethnic groups, with 56% of all women admitted being from a black and minority ethnicity background. 70% of women who required admission had a raised body mass index (BMI) and 30% had comorbidities including pre-existing cardiorespiratory disease, which may indicate an increased risk of more severe disease in these groups.

The symptoms that pregnant women reported at presentation to hospital were also described. The leading symptoms were fever, cough and breathlessness, which mirror those of the non-obstetric population.¹²

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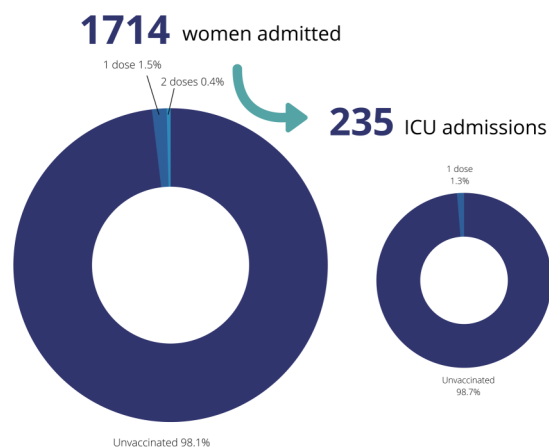


Figure 1. Women admitted with symptomatic COVID-19 in pregnancy between 1st February 2021 to 30th September 2021 in the UK and their vaccination status.

Maternal mortality

Data on the 8 pregnant and 2 postnatal women who died in the UK with COVID-19 during the first wave of the pandemic, between 1st March 2020 and 31st May 2020, was collected and reported by MBRRACE-UK, who calculated a maternal mortality rate of 6.2 per 100,000 from COVID-19.¹³ All 8 of the women who died during pregnancy were in the third trimester. Demographic data showed 7 of these women were from a black and minority ethnicity background, supporting the observational studies in non-pregnant individuals, which showed black and minority ethnicity to be a risk factor for both COVID-19 and mortality.¹⁴

The 2021 rapid report from the MBRRACE-UK group included a further 14 women who died with COVID-19 during pregnancy or up to a year postpartum, in the period between 1st June 2020 and 31st March 2021.¹⁵ Findings from this report echo those of the initial report, with 60% of the 10 women who died being from a black and minority ethnicity group, 80% having a raised BMI and 50% presenting in their third trimester. No women smoked or were identified as having pre-existing diabetes, hypertension or cardiac disease. The maternal mortality rate calculated from this group was 2.4 per 100,000 (95% CI 1.3–4.0).

The recommendations from both MBRRACE reports highlight the importance of multidisciplinary input to determine place of care, escalation of care, the need to consider if iatrogenic preterm delivery to improve maternal ventilation and oxygenation is indicated and noted that pregnant women are at risk of rapid deterioration from COVID-19.

Cerebral thromboembolism was found to be the cause of death in one case, leading to the recommendation for venous thromboembolism risk assessment for pregnant women admitted with SARS CoV-2 infection on diagnosis, during admission and on discharge.

It was also noted that 3 women presented late in the course of their illness or died at home due to what they perceived to be the risk of attending hospital. Although social distancing and shielding in high-risk groups remains advisable, a clear message regarding the importance of recognising ‘red flag’ symptoms for clinicians and patients as well as clear pathways for the care of pregnant women may reduce preventable deaths from COVID-19.

Review of the care received by the women that died revealed that some pregnant women were not offered steroids or were deemed unsuitable for other treatments due to pregnancy, despite them being in line with available evidence and guidance at the time, including extracorporeal membrane oxygenation (ECMO).

During the third wave of the pandemic, between July 2021 and September 2021, a further 13 women died during pregnancy or up to 6

weeks postpartum,⁵ demonstrating the ongoing need for data collection to inform decision making and specialised care.

Outcomes of pregnant women with COVID-19

A multinational prospective cohort study on 2130 women looked at the incidence of adverse maternal and neonatal outcomes in pregnant women with both symptomatic and asymptomatic SARS CoV-2 infection over an eight month period from 2nd March 2020.⁶ The study, carried out across 18 centres, compared a cohort of pregnant women with SARS CoV-2 to a similar cohort of pregnant women without evidence of infection. Analysis of the data collected demonstrated an increased risk of hypertensive disease including gestational hypertension (RR, 1.46; 95% CI, 1.05–2.02) and preeclampsia/eclampsia/hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome (RR, 1.76; 95% CI, 1.27–2.43) in pregnant women with SARS CoV-2 infection. Infection was demonstrated to be a risk factor for both hospital admission and ICU admission in pregnancy, with women who had COVID-19 having longer ICU stays than those without. 12 women died during the study, 11 of which were in the COVID group. SARS CoV-2 infection in pregnancy is associated with greater maternal mortality (RR, 22.3; 95% CI, 2.88–172). The maternal mortality ratio calculated was 159 per 10 000 births.

SARS CoV-2 infection in pregnancy was also shown to be associated with an increased risk of preterm birth of which 83% were iatrogenic. Indications for iatrogenic preterm delivery in this group included maternal hypertensive disease (24.7%), small for gestational age (SGA) (15.5%) and fetal distress (13.2%).

A recent population-based cohort study conducted in the UK between 29th May 2020 and 31st January 2021, including 3527 SARS CoV-2 positive pregnant women, also found an association between SARS CoV-2 infection and preterm birth, stillbirth, preeclampsia and caesarean birth.¹⁶

Data from these studies indicate that SARS CoV-2 infection affects pregnancy beyond just maternal respiratory compromise and is associated with poorer pregnancy outcomes, including SGA babies, hypertensive disease and stillbirth, therefore preventing transmission to this population may reduce some of the preventable complications described.

Over the course of the pandemic, 3 predominant variants of SARS CoV-2 were identified in the UK, the Wildtype (dominant from March 2020 – November 2020), the Alpha variant (dominant from December 2020 – May 2021) and the Delta variant (dominant from May 2021 to July 2021). A UK-based prospective cohort study examined the association between each variant and disease severity and outcomes in pregnancy.³ Data obtained from UKOSS was used in analysis of 3371 symptomatic pregnant women with COVID-19 and demonstrated an association between more severe disease and the Alpha and Delta variants, compared to the Wildtype. The incidence of moderate to severe infection between the Wildtype and Alpha period was significant at 24.4% versus 35.8% (aOR1.75 95%CI 1.48–2.06) and between the Alpha and Delta was 35.8% versus 45.0% (aOR1.53, 95%CI 1.07–2.17). Pregnant women were found to be more likely to require respiratory support, hospital admission, admission for level 3 care and have radiological evidence of COVID pneumonia, with the Delta variant (compared to the Alpha variant and Wildtype variant).

Discussion

Respiratory manifestations of SARS CoV-2 are well documented, but as we learn more about the infection in pregnancy, it is clear that there are significant placental and fetal consequences of even mild infection.¹⁷ Placental complications may be the cause of the increased risk of SGA,

hypertensive disease and stillbirth, although the mechanisms remain unclear. Given the increased risk, there may be an indication for additional antenatal surveillance and follow-up in these women to detect, treat and potentially prevent these complications. Pressures on services including staff and bed shortages mean that pathways are required in outpatient and community care to follow up women who contract COVID-19 during pregnancy. Further research is required to better understand the pathophysiology of SARS CoV-2 in pregnancy and whether long COVID may affect future pregnancies.

The care of women who died of COVID-19 in the UK was noted to be lacking in some cases where inadequate senior obstetric input was sought and a shortage of beds in a level 3 setting delayed the initiation of the respiratory support required. This reinforces the recommendation for multidisciplinary care for pregnant women with COVID-19, to improve their access to treatment and reduce preventable deaths that may be related to the healthcare provider's unfamiliarity with COVID-19 in pregnancy and recognition of a deteriorating pregnant woman. Despite clear associations with women of a black and minority ethnicity background, it is not clear from the research reviewed why ethnicity is a risk factor for COVID infection and mortality. Historical MBRRACE-UK reports have found that black and minority ethnicity pregnant women are more likely to die during pregnancy and in the postpartum period^{18,19} raising the possibility that the same underlying factors such as healthcare inequality as a result of structural racism²⁰ are playing a role in the poorer outcomes of black and minority ethnicity pregnant women who contract COVID-19.

Conclusion

In conclusion, SARS CoV-2 infection can cause severe pneumonia and respiratory failure in pregnant and postnatal women leading to hospital admission, most commonly in the later stages of pregnancy and peripartum and, in some cases, requiring enhanced levels of cardiorespiratory support.^{2,21} COVID-19 in pregnant women presenting to secondary care most commonly presents similarly to the non-obstetric population with fever, cough and breathlessness as the leading symptoms. The current data available demonstrate that infection in pregnancy is associated with an increased risk of stillbirth, preterm birth, SGA and preeclampsia,⁶ which may support an indication for additional surveillance for these conditions following COVID infection. The evidence examined also suggests that black and minority ethnicity background is a risk factor for both COVID-19, maternal mortality and poorer outcomes overall,^{2,11–13} highlighting the need for further research in this group.

Data from UKOSS demonstrated that none of the pregnant women admitted to hospital up to 11th July 2021 had received both doses of the COVID vaccine⁴ and between February 2021 and September 2021 only 0.4% of pregnant women admitted were fully vaccinated.⁵ Vaccination as a strategy to reduce the incidence, transmission and disease severity is therefore likely to reduce hospital admissions and improve outcomes from COVID-19 in pregnant women. Ensuring access to antenatal care, including face to face contact where necessary, allows for screening and diagnosis of COVID-related obstetric complications. In addition, reducing the exposure of pregnant women to SARS CoV-2 through social distancing and other strategies remain crucial.

Ongoing surveillance and research on COVID-19 in pregnancy are imperative. The implications of long COVID on current and future pregnancies, in particular, is a major area of uncertainty and concern. New knowledge and the recommendations that can be derived from it will be invaluable in guiding clinical care in future COVID-19 outbreaks, the emergence of new variants and against other novel respiratory viruses.

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