



Coronavirus in pregnancy and delivery: rapid review

E. MULLINS¹ , D. EVANS^{2,3}, R. M. VINER^{3,4}, P. O'BRIEN^{5,6} and E. MORRIS^{6,7}

¹Department of Metabolism, Digestion and Reproduction, Imperial College London, Queen Charlotte's and Chelsea Hospital, London, UK; ²North Bristol NHS Trust, Bristol, UK; ³The Royal College of Paediatrics and Child Health, London, UK; ⁴University College London, London, UK; ⁵University College London Hospitals NHS Foundation Trust, London, UK; ⁶The Royal College of Obstetricians and Gynaecologists, London, UK; ⁷Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, Norfolk, UK

KEYWORDS: breastfeeding; COVID-19; fetal; miscarriage; neonatal; pregnancy; preterm birth

CONTRIBUTION

What are the novel findings of this work?

This is the most up-to-date review of COVID-19 in pregnancy, with comparison to previous outbreaks of novel coronavirus in pregnancy. We discuss the limited data available, the limited evidence base for clinical practice, possible therapeutic options in pregnancy and future research.

What are the clinical implications of this work?

A version of this rapid review, with searches up to 25 February 2020, informed the Royal College of Obstetricians and Gynaecologists' guidance on COVID-19 in pregnancy.

ABSTRACT

Objectives There are limited case series reporting the impact on women affected by coronavirus during pregnancy. In women affected by severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), the case fatality rate appears higher in those affected in pregnancy compared with non-pregnant women. We conducted a rapid review to guide health policy and management of women affected by COVID-19 during pregnancy, which was used to develop the Royal College of Obstetricians and Gynaecologists' (RCOG) guidelines on COVID-19 infection in pregnancy.

Methods Searches were conducted in PubMed and MedRxiv to identify primary case reports, case series, observational studies and randomized controlled trials describing women affected by coronavirus in pregnancy. Data were extracted from relevant papers. This review has been used to develop guidelines with representatives of the Royal College of Paediatrics and Child Health

(RCPCH) and RCOG who provided expert consensus on areas in which data were lacking.

Results From 9965 search results in PubMed and 600 in MedRxiv, 21 relevant studies, all of which were case reports or case series, were identified. From reports of 32 women to date affected by COVID-19 in pregnancy, delivering 30 babies (one set of twins, three ongoing pregnancies), seven (22%) were asymptomatic and two (6%) were admitted to the intensive care unit (ICU), one of whom remained on extracorporeal membrane oxygenation. No maternal deaths have been reported to date. Delivery was by Cesarean section in 27 cases and by vaginal delivery in two, and 15 (47%) delivered preterm. There was one stillbirth and one neonatal death. In 25 babies, no cases of vertical transmission were reported; 15 were reported as being tested with reverse transcription polymerase chain reaction after delivery. Case fatality rates for SARS and MERS were 15% and 27%, respectively. SARS was associated with miscarriage or intrauterine death in five cases, and fetal growth restriction was noted in two ongoing pregnancies affected by SARS in the third trimester.

Conclusions Serious morbidity occurred in 2/32 women with COVID-19, both of whom required ICU care. Compared with SARS and MERS, COVID-19 appears less lethal, acknowledging the limited number of cases reported to date and that one woman remains in a critical condition. Preterm delivery affected 47% of women hospitalized with COVID-19, which may put considerable pressure on neonatal services if the UK's reasonable worst-case scenario of 80% of the population being affected is realized. Based on this review, RCOG, in consultation with RCPCH, developed guidance for delivery and neonatal care in pregnancies affected by COVID-19, which recommends that delivery

Correspondence to: Dr E. Mullins, Department of Metabolism, Digestion and Reproduction, Imperial College London, Queen Charlotte's and Chelsea Hospital, DuCane Road London, London W12 0HS, UK (e-mail: edward.mullins@imperial.ac.uk)

Accepted: 13 March 2020

mode be determined primarily by obstetric indication and recommends against routine separation of affected mothers and their babies. We hope that this review will be helpful for maternity and neonatal services planning their response to COVID-19. © 2020 The Authors. *Ultrasound in Obstetrics & Gynecology* published by John Wiley & Sons Ltd on behalf of the International Society of Ultrasound in Obstetrics and Gynecology.

INTRODUCTION

The common human coronaviruses 229E (alpha coronavirus), NL63 (alpha coronavirus), OC43 (beta coronavirus) and HKU1 (beta coronavirus) cause the common cold. Three human coronaviruses cause more severe, acute illnesses; MERS-CoV causes Middle East respiratory syndrome (MERS), SARS-CoV causes severe acute respiratory syndrome (SARS) and SARS-CoV-2 causes COVID-19.

There are limited case series reporting on the impact of coronaviruses during pregnancy. In women affected by SARS or MERS, the case fatality rate appeared higher in those affected in pregnancy compared with non-pregnant women.

Person-to-person spread of COVID-19 in the UK has now been confirmed. To guide treatment and prevention in women affected by COVID-19 during pregnancy in the current outbreak, we conducted a rapid review.

METHODS

Searches were conducted in PubMed and MedRxiv on 25 February 2020 (Appendix S1) and updated on 10 March to identify primary case reports, case series and randomized controlled trials describing women of any age affected by coronavirus in pregnancy or the postnatal period. There were no date or language restrictions on the search. References of relevant papers were searched manually for relevant studies.

Due to time constraints, one reviewer (E.M.) conducted the search, reviewed full texts and extracted data on demographics, maternal outcomes, maternal diagnostic testing, maternal imaging, fetal, perinatal and neonatal outcomes, and neonatal diagnostic testing. Comparison of outcomes between pregnancies affected by COVID-19, SARS and MERS is presented.

The review was not registered in PROSPERO and corresponding authors were not contacted due to time constraints. The quality of included studies was assessed subjectively and classified as anecdotal, low, medium or high. Ethical approval was not required for this review.

This review has been used to develop interim guidance on COVID-19 infection in pregnancy, with representatives of the Royal College of Paediatrics and Child Health (RCPCH) and the Royal College of Obstetricians and Gynaecologists (RCOG) providing expert consensus on areas in which data were lacking. This guidance has now been published in full by RCOG¹.

RESULTS

The search of PubMed identified 9965 results; 69 abstracts were screened, of which 48 were excluded due to the study not including pregnant women or humans, or being an *in-vitro* study. Twenty-one relevant studies were identified^{2–22}; their full texts were reviewed and all 21 were included. It is highly likely that there was overlap in cases reported to be affected by SARS. The search of MedRxiv identified 600 results; 39 abstracts were screened and no relevant studies were identified.

All studies were case reports or series and all were classified subjectively as being of low quality. There was inconsistent reporting of maternal, perinatal and neonatal outcomes. Outcomes of included cases are summarized in Table 1. A narrative review is presented.

Maternal outcome

COVID-19. To date, 32 women affected by COVID-19 in pregnancy, including one with a twin pregnancy, have been reported, delivering 30 infants (three pregnancies were ongoing)^{2–5}. Twenty-seven delivered by Caesarean and two by vaginal delivery. Women who delivered did so within 13 days of onset of illness. In cases in which maternal morbidity and mortality were reported ($n=23$), two women required intensive care unit (ICU) admission and mechanical ventilation, one of whom developed multiorgan dysfunction and was still on extracorporeal membrane oxygenation (ECMO) when the case was reported. When reported ($n=17$), all symptomatic women had viral changes apparent on computed tomographic (CT) chest imaging. There were no maternal deaths to date^{2,3}.

SARS. The case fatality rate (CFR) was 15% for all reported cases of SARS in pregnancy^{6–11}. A case-control study comparing 10 pregnant and 40 non-pregnant women affected by SARS in Hong Kong reported an ICU admission rate of 60% and a CFR of 40% in the pregnant group, compared with respective values of 17.5% and 0% in the non-pregnant group⁹. All women affected by SARS had CT or chest X-ray evidence of pneumonia (Table 2).

MERS. In pregnant women affected by MERS, 7/11 (64%) were admitted to the ICU, and CFR was 3/11 (27%)^{12–17}.

Early pregnancy

COVID-19. There are currently no data on first-trimester COVID-19 infection.

SARS. Miscarriage affected 4/7 women with first-trimester SARS infection⁸, all of whom had an ultrasound finding at 3–5 weeks of pregnancy of unknown location or unknown viability, in which ongoing pregnancy at 13 weeks would be expected in 38% and 50%, respectively, acknowledging the complexity in this area^{23,24}. Those with fetal heart activity recorded ($n=2$) did not miscarry, neither did a woman in whom the diagnosis was retrospective and did not undergo ultrasound examination.

Table 1 Overview of pregnancy and perinatal and neonatal outcomes in pregnancies affected by coronaviruses, according to gestational age (GA) at diagnosis

Variable	COVID-19 ^a			SARS				MERS			
	All	Second trim	Third trim	All	First trim	Second trim	Third trim	All	First trim	Second trim	Third trim
<i>n</i>	32 ^b	2	30	20 ^h	7	5	8	11	1	5	5
Maternal age (years)	30 (25–40)			31 (24–44)				33 (27–39)			
GA at presentation (weeks)	36.5 (25–39)			16 (3–32)				24 (6–38)			
Maternal comorbidity	4/19 (21) ^c	NR	4/19 (21) ^c	NR	NR	NR	NR	5 (45)	0 (0)	2 (40)	3 (60)
Asymptomatic at admission	7 (22)	2 (100)	5 (17)	0 (0)	0 (0)	0 (0)	0 (0)	2 (18)	1 (100)	1 (20)	0 (0)
ICU admission	2/23 (9) ^d	0 (0)	2/21 (10) ^d	6 (30)	1 (14)	2 (40)	3 (38)	7 (64)	0 (0)	3 (60)	4 (80)
Maternal mortality	0 (0) ^{c,d}	0 (0)	0 (0) ^{c,d}	3 (15)	1 (14)	1 (20)	1 (13)	3 (27)	0 (0)	1 (20)	2 (40)
Viral changes on chest CT/X-ray in symptomatic women	18/19 (95) ^c			20 (100)				8/9 (89) ^k			
Miscarriage or IUD	1 (3) ^e	0 (0) ^e	1 (3) ^e	5 (25)	4 (57)	0	1 (13) ^j	2 (18)	0 (0)	1 (20)	1 (20)
Preterm delivery											
Any	15 (47) ^f	0 (0) ^f	15 (50) ^f	4/13 (31) ⁱ	NR	2 (40) ⁱ	2 (25) ⁱ	3 (27)	0 (0)	1 (20)	2 (40)
Spontaneous	0 (0)	0 (0)	0 (0) ^d	1 (5) ⁱ	NR	0 (0) ⁱ	1 (13) ⁱ	0 (0)	0 (0)	0 (0)	0 (0)
Post-infection FGR	NR	NR	NR	2 (10)	NR	0 (0)	2 (25)	0 (0)	0 (0)	0 (0)	0 (0)
Vertical transmission	0/25 (0) ^g	—	0/25 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Neonatal death	1/29 (3)	—	1/29 (3)	0/13 (0)	NR	0 (0)	0 (0)	1 (9)	0 (0)	1 (20)	0 (0)

Data are given as median (range), *n* (%) or *n/N* (%). ^aNo reported cases of first-trimester COVID-19 infection identified. ^bIncluding two ongoing pregnancies diagnosed with COVID-19 in second trimester and one ongoing and one twin pregnancy diagnosed in third trimester, giving total of 30 babies delivered. ^cIncomplete data from Liu *et al.*⁵. ^dIncomplete data from Zhu *et al.*⁴. ^eFetuses in ongoing pregnancies were assumed to survive. ^fOngoing pregnancies were assumed to deliver at term, based on clinical prognosis. ^gNot all infants were tested and some pregnancies were ongoing. ^hIncluding one twin pregnancy diagnosed with SARS in third trimester. ⁱData (*n* = 5) on timing of delivery not reported by Zhang *et al.*¹⁹ but all were assumed to deliver at term. ^jOccurred in twin pregnancy. ^kOne woman declined radiography because of concerns about effect on pregnancy and one woman was asymptomatic in first trimester. CT, computed tomography; FGR, fetal growth restriction; ICU, intensive care unit; IUD, intrauterine death; MERS, Middle East respiratory syndrome; NR, not reported; SARS, severe acute respiratory syndrome; trim, trimester.

MERS. A single case of a woman with MERS in the first trimester has been reported. This woman was asymptomatic and went on to have a term delivery¹⁸.

Second/third-trimester pregnancy loss

COVID-19. One woman affected by COVID-19 presented at 34 weeks with a fever and sore throat; her condition deteriorated during admission and she required admission to the ICU and ECMO⁵. The woman had a stillbirth, delivered by Cesarean section. No information on chronology or fetal monitoring was reported.

SARS. In cases of SARS reported after the first trimester, Zhang *et al.* reported a series of five women affected by SARS (two in the second trimester, three in third trimester) in which there was loss of one fetus in a twin pregnancy with the other surviving to delivery. It is not clear if the loss occurred in the second or third trimester; this has been recorded arbitrarily as occurring in the third trimester¹⁹.

MERS. Two pregnancy losses were reported in pregnancies affected by MERS. In the first case, the woman became ill at 19 weeks gestation and experienced vaginal bleeding resulting in late fetal loss at 20 weeks¹⁷. It should be noted that this woman declined chest radiography and medication because of her concerns about their effect on pregnancy. The second case presented at 34 weeks with pre-eclampsia and MERS and was found

to have had an intrauterine death; this woman delivered vaginally and recovered after ICU admission without ventilatory support¹⁴.

Prematurity

COVID-19. Fifteen of the 32 (47%) women affected by COVID-19 delivered preterm. In the study of Chen *et al.*, all (*n* = 9) mothers were delivered electively by Cesarean section, two of which were at 36 weeks' gestation². In the study of Zhu *et al.*, seven women delivered by Cesarean section and two by vaginal delivery⁴; 5/9 women (6/10 babies) delivered preterm. The indication for delivery is not reported; however, six babies were affected by fetal distress prior to delivery and it seems reasonable to assume that fetal condition contributed. Wang *et al.* reported on one woman who delivered at 30 weeks for fetal distress³. Liu *et al.* reported on 13 women, of whom seven delivered preterm by Cesarean section; indication for delivery was not reported⁵.

SARS. Four of the 16 SARS pregnancies that were not affected by miscarriage resulted in preterm delivery at 26, 28, 32 and 33 weeks' gestation, respectively¹⁸. Data on timing of delivery were not reported in the series of five women from Zhang *et al.*¹⁹.

Table 2 Details of women affected by coronavirus in pregnancy who died, as of 6 March 2020

Corona-virus	MA (years)	GA (weeks)	Clinical presentation	Comorbidity	Chest imaging	Progression	Delivery and neonatal outcome	Cause of maternal death
SARS ⁸	44	5	Cough, headache, SOB, chills	NR	Pneumonia	Secondary bacterial pneumonia, DIC, renal failure, ARDS	Miscarriage	Respiratory failure
	34	32	Myalgia, cough, chills	NR	Pneumonia	Sepsis, ARDS, shock, abdominal wound dehiscence	CS, neonatal survival	Respiratory failure
	34	27	Myalgia, cough, headache, SOB, sore throat	NR	Pneumonia	Secondary bacterial pneumonia, DIC, ARDS, abdominal wound dehiscence	CS, ARDS, NEC, neonatal survival	MRSA pneumonia
MERS ²⁰	32	38	Fever, cough, SOB	None	Bilateral infiltrates (chest X-ray)	Worsening pneumonia, renal failure, ARDS	Spontaneous vaginal delivery, neonatal survival	Multiorgan failure
	31	24	Cough, myalgia	Asthma, pulmonary fibrosis, spontaneous pneumothoraces	Right lower lobe opacity	Worsening pneumonia, ARDS	Emergency CS for maternal hypoxemia, neonatal death	Severe refractory hypoxia, cardiac arrest
	32	32	Fever, back pain	None	Bilateral consolidation (CT)	Septic shock	Emergency CS for maternal hypoxemia, neonatal death	Septic shock

There were no maternal deaths in COVID-19 cases. ARDS, acute respiratory distress syndrome; CS, Cesarean section; CT, computed tomography; DIC, disseminated intravascular coagulation; GA, gestational age; MA, maternal age; MERS, Middle East respiratory syndrome; MRSA, methicillin-resistant *Staphylococcus aureus*; NEC, necrotizing enterocolitis; NR, not reported; SARS, severe acute respiratory syndrome; SOB, shortness of breath.

MERS. Three of the 11 pregnancies with MERS were delivered preterm by Cesarean section (one at 24 weeks and two at 32 weeks for maternal hypoxemia)^{12,18}.

Fetal growth and placental effects

COVID-19. Women affected by COVID-19 who delivered did so within 13 days of onset of illness^{2–5}; fetal growth is unlikely to be affected in this time period. There were no data on fetal growth in the three ongoing pregnancies at the time of publication⁵. No placental pathology is available to date.

SARS. Placentas from pregnancies affected by SARS showed early changes (fibrin deposition), that are seen in pregnancies with fetal growth restriction, when delivery occurred ≤ 1 week after onset of illness; birth weight was normal in these pregnancies²⁰. When delivery was 5–7 weeks after onset of illness, there was fetal growth restriction in 2/3 pregnancies⁸ and their placentas showed more severe changes (areas with loss of blood supply, avascular villi, bleeding behind the placenta, placental abruption)²⁰.

MERS. Four of the 11 women with MERS went on to deliver a healthy baby at term, although birth weight was not reported in 3/4 of these cases. In one case, vaginal bleeding was reported at 37 weeks, causing fetal compromise and necessitating emergency Cesarean section resulting in the delivery of a male infant weighing 3140 g and in good condition. Abruption was apparent on placental examination¹³.

Delivery and postnatal

COVID-19. Chen *et al.* reported on nine women with COVID-19 delivering by Cesarean section from 36 weeks onwards, of which two were preterm. In two women at term, fetal distress was reported. In six women with COVID-19 who delivered by Cesarean section and subsequently underwent testing, there was no evidence of COVID-19 in the amniotic fluid, umbilical cord blood, neonatal throat swab or breast milk samples². A news report of a baby of a COVID-19-infected mother testing positive at 30 h after delivery has not been reported in a

scientific journal. Zhu *et al.* reported COVID-19 in nine women delivering 10 infants (seven by Cesarean section and two by vaginal delivery), of whom only three mothers became symptomatic after delivery. The indication for delivery was not reported. This cohort had COVID-19 from 31 weeks onwards, 6/9 pregnancies showed fetal distress and 5/9 women (6/10 babies) delivered preterm⁴. Wang *et al.* reported on one woman who underwent Cesarean section for fetal distress at 30 weeks' gestation. The infant was born in good condition and samples of amniotic fluid, neonatal gastric samples, placenta and infant throat swabs were negative for COVID-19³. Liu *et al.* reported on 10 women, all of whom delivered by Cesarean section. Vertical transmission was reported as negative in all 10 neonates. The samples and method of testing is not stated⁵.

SARS and MERS. No vertical transmission was reported for cases of SARS or MERS in pregnancies delivered by Cesarean section or vaginal delivery.

Other coronaviruses. A single case series reported on neonates born to mothers who were positive for HCoV-229E; gastric samples in three out of seven cases were positive for HCoV-229E on reverse transcription polymerase chain reaction (RT-PCR); seroconversion was not assessed. No signs of infant infection were seen in those with positive gastric samples²¹.

Neonatal outcome

COVID-19. In the study of Chen *et al.*, all ($n = 9$) babies were delivered ≥ 36 weeks' gestation and were well at discharge². Zhu *et al.* reported on a cohort delivered at an earlier gestational age (from 31 weeks); 6/10 babies were admitted to the neonatal unit for respiratory support, two developed disseminated intravascular coagulation (DIC) and one had multiple organ failure⁴. Neonatal morbidity was more marked in this series, probably due to greater prematurity. One baby died after being born at 34 weeks. The neonate required admission at 30 min after delivery with respiratory difficulties. The baby's condition deteriorated, and it developed shock, DIC and multiple organ failure, and died at 8 days postpartum. Nine of the 10 infants were tested for COVID-19, all of which tested negative. Wang *et al.* reported on a baby born at 30 weeks in good condition with an uneventful neonatal course³. Liu *et al.* reported on one stillborn and nine liveborn neonates, all of which had an Apgar score (time unspecified) of 10^5 .

SARS. Among pregnancies affected by SARS, a baby born at 26 weeks had respiratory distress syndrome (RDS) and a bowel perforation. In another case, a baby born at 28 weeks had RDS, necrotizing enterocolitis and a patent ductus arteriosus^{8,11}.

MERS. Among the three MERS pregnancies that were not affected by stillbirth or intrauterine death and that were delivered preterm by Cesarean section, one delivered at 24 weeks and resulted in neonatal death (birth weight, 240 g) and the other two delivered at 32 weeks for maternal hypoxemia and have no outcomes reported^{12,20}.

DISCUSSION

There are limited data on the impact of the current COVID-19 outbreak on women affected in pregnancy and their babies. All studies included in this review were case reports or series of low quality. Reported outcomes varied, with one series on COVID-19 not reporting maternal outcome.

Of the 23/32 women with COVID-19 in pregnancy for whom maternal outcomes were reported, two had serious morbidity, one of whom was still on ECMO following stillbirth, at the time her care was reported. Compared with SARS and MERS, COVID-19 appears to be less lethal, although acknowledging the limited number of cases reported to date and that one woman remains in a critical condition. Preterm delivery affected 47% of women hospitalized with COVID-19, which may put considerable pressure on neonatal services if the UK's reasonable worst-case scenario of 80% of the population being affected is realized.

RCOG, in consultation with the RCPCH, have provided guidance for delivery and neonatal care, which recommends that delivery mode be determined primarily by obstetric indication, and recommends against routine separation of COVID-19-affected mothers and their babies¹.

From the currently available data, an increase in the risk of miscarriage in women affected by COVID-19 cannot be ruled out at this stage, given the SARS data. Data from early pregnancy units are needed on affected women and matched controls.

In women affected by COVID-19 with ongoing pregnancy, surveillance for fetal growth restriction would be reasonable, given the acute and chronic placental changes observed in SARS pregnancies and with 2/3 of those that were ongoing being affected by fetal growth restriction after SARS infection, and that placental abruption was noted in a case affected by MERS.

The need for provision of fetal monitoring, including serial ultrasound examination, of women with COVID-19 will be challenging for maternity services. Women will need to be monitored locally in their booking maternity units, with transfer to centers with appropriate neonatal intensive care facilities for delivery. COVID-19 is associated with preterm delivery in 47% of reported cases.

In SARS and MERS-affected cases, delivery was most often indicated by maternal hypoxemia. In COVID-19, if maternal illness is not as severe, the considerations will be based more on obstetric indications for delivery.

Information on vertical transmission of COVID-19 is limited, although testing of 15 neonates born to mothers with COVID-19 was negative in all cases. Guidance on mode of delivery requires expert consensus until further information emerges. RCOG advises that decisions regarding mode of delivery should be on obstetric indication and not on presumed protection of the baby against infection. There is evidence for vertical transmission of HCoV-229E; however, seroconversion was not investigated and all infants remained well²¹. There is no evidence for vertical transmission for any other coronavirus.

We acknowledge the limitations of this review, given that a full and comprehensive search of all medical literature would have taken more time and personnel than were available. We used a single reviewer and a limited database search in order to conduct this rapid review.

There is discrepancy between guidance for delayed cord clamping, which is a function of a lack of evidence. Consensus guidance from China advises that 'delayed cord clamping is not recommended', in order to reduce the risk of vertical transmission, and that infants should be separated from mothers affected by COVID-19²⁵. Interim guidance from ISUOG advises clinicians to consider not undertaking delayed cord clamping²⁶. RCOG guidance does not concur, advising that delayed cord clamping should be practiced as normal. If vaginal delivery is permitted, with exposure to maternal secretions and blood, it could be argued that 1 min of further perfusion via the placenta is unlikely to alter the risk of vertical transmission. Infants may acquire COVID-19 from their mothers after delivery via normal routes of transmission.

Guidance from China states that 'Infants should not be fed with the breast milk from mothers with confirmed or suspected 2019-nCoV'. Guidance from the Centers for Disease Control and Prevention is less clear but is still precautionary²⁷. RCOG advises against routine separation of mother and baby and gives guidance on individualized care.

If the UK's reasonable worst-case scenario of 80% of the population being affected by COVID-19 is realized and 4% require hospitalization, thousands of pregnant women will potentially be affected at a time at which staff are likely themselves to be unwell. In previous coronavirus epidemics, there has anecdotally been a tendency towards admitting any symptomatic pregnant woman with proven infection.

A surge in workload will likely be seen in healthcare services across the world at a time at which staffing is well below optimal levels. Pragmatic choices will need to be made about achievable and acceptable levels of care according to national guidance and local adaptation. Chest imaging should be undertaken in pregnant women as clinically indicated.

Therapeutics announced as being under consideration and trial during the outbreak include Kaletra (lopinavir and ritonavir), remdesivir and chloroquine. Kaletra²⁸ is used in the UK during pregnancy for treatment of HIV, in which the benefits of treatment outweigh the risks of toxicity seen in animal studies. The benefits of using chloroquine outweigh the risks in the prevention and treatment of malaria during pregnancy²⁹. Remdesivir has been used for the treatment of Ebola in pregnant women³⁰. However, it should be acknowledged that Ebola is a condition with a CFR of 50%, and for which there would be higher tolerance for adverse effects of a potentially beneficial treatment than would be the case for COVID-19, in which the CFR is around 1%. It would seem reasonable not to exclude seriously ill pregnant women from trials of these therapies for COVID-19.

There is a need for systematic data reporting on women affected by COVID-19 and their pregnancies to provide an evidence base for management, treatment and prevention, and to target limited resources during the outbreak.

DISCLOSURE

E.M. is seconded to the Department of Health and Social Care (DHSC), England. The views in this manuscript are those of the authors and do not necessarily represent the official views of DHSC or HM Government. E.M. has applied for a UKRI/MRC grant to study COVID-19 in pregnancy. No other authors have conflicts of interest to declare. E.M. received a salary from the NIHR.

REFERENCES

- Royal College of Obstetricians and Gynaecologists. Coronavirus (COVID-19) infection and pregnancy. <https://www.rcog.org.uk/globalassets/documents/guidelines/coronavirus-covid-19-infection-in-pregnancy-v3-20-03-18.pdf>
- Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, Li J, Zhao D, Xu D, Gong Q, Liao J, Yang H, Hou W, Zhang Y. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet* 2020; **6736**: 1–7.
- Wang X, Zhou Z, Jianping Z, Zhu F, Tang Y, Shen X. A case of 2019 Novel Coronavirus in a pregnant woman with preterm delivery. *Clin Infect Dis* 2020. DOI: 10.1093/cid/ciaa200.
- Zhu H, Wang L, Fang C, Peng S, Zhang L, Chang G, Xia S, Zhou W. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr* 2020; **9**: 51–60.
- Liu Y, Chen H, Tang K, Guo Y. Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy. *J Infect* 2020. DOI: 10.1016/j.jinf.2020.02.028.
- Robertson CA, Lowther SA, Birch T, Tan C, Sorhage F, Stockman L, McDonald C, Lingappa JR, Bresnitz E. SARS and Pregnancy: A Case Report. *Emerg Infect Dis* 2004; **10**: 345–348.
- Li AM, Ng PC. Severe acute respiratory syndrome (SARS) in neonates and children. *Arch Dis Child Fetal Neonatal Ed* 2005; **90**: 461–465.
- Wong SF, Chow KM, Leung TN, Ng WF, Ng TK, Shek CC, Ng PC, Lam PW, Ho LC, To WW, Lai ST, Yan WW, Tan PY. Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. *Am J Obstet Gynecol* 2004; **191**: 292–297.
- Lam CM, Wong F, Leung N, Chow M. A case-controlled study comparing clinical course and outcomes of pregnant and non-pregnant women with severe acute respiratory syndrome. *BJOG*; 2004; **111**: 771–774.
- Schwartz D, Graham A. Potential Maternal and Infant Outcomes from Coronavirus 2019-nCoV (SARS-CoV-2) Infecting Pregnant Women: Lessons from SARS, MERS, and Other Human Coronavirus Infections. *Viruses* 2020; **20**: 1–16.
- Shek CC, Ng PC, Fung GPG, Cheng FWT, Chan PKS, Peiris MJS, Lee KH, Wong SF, Cheung HM, Li AM, Hon EK, Yeung CK, Chow CB, Tam JS, Chiu MC, Fok TF. Infants Born to Mothers With Severe Acute Respiratory Syndrome. *Pediatrics* 2020; **112**: e254.
- Alserehi H, Wali G, Alshukairi A, Alraddadi B. Impact of Middle East Respiratory Syndrome coronavirus (MERS-CoV) on pregnancy and perinatal outcome. *BMC Infect Dis* 2016; **16**: 1–4.
- Jeong SY, Sung SJ, Sung J, Ahn SY, Kang E, Chang YS, Park WS, Kim JH. MERS-CoV Infection in a Pregnant Woman in Korea. *J Korean Med Sci* 2017; **3**: 5–8.
- Assiri A, Abedi G, Malak M, Abdulaziz B, Gerber S, Watson JT. Pregnancy: A Report of 5 Cases From Saudi Arabia. *Clin Infect Dis* 2016; **63**: 951–953.
- Park MH, Kim HR, Choi DH, Sung JH, Kim JH. Emergency cesarean section in an epidemic of the middle east respiratory syndrome. *Korean J Anesthesiol* 2016; **69**: 287–291.
- Malik A, Medhat K, Masry E, Ravi M, Sayed F. Middle East Respiratory Syndrome Coronavirus during Pregnancy, Abu Dhabi, United Arab Emirates, 2013. *Emerg Infect Dis* 2016; **22**: 515–517.
- Payne D, Ibrahim I, Sultan A. Stillbirth During Infection With Middle East Respiratory Syndrome Coronavirus. *J Infect Dis* 2014; **209**: 1870–1872.
- Alfaraj S, Al-Twfiq J, Memish Z. Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection during pregnancy: Report of two cases & review of the literature. *J Microbiol* 2019; **52**: 501–503.
- Zhang J, Wang Y, Chen L, Zhang R, Xie Y. Clinical analysis of pregnancy in second and third trimesters complicated severe acute respiratory syndrome. *Zhonghua Fu Chan Ke Za Zhi* 2003; **38**: 516–520.
- Ng WF, Wong SF, Lam A, Mak YF, Yao H, Lee KC, Chow KM, Yu WC, Ho LC. The placentas of patients with severe acute respiratory syndrome: A pathophysiological evaluation. *Pathology* 2006; **38**: 210–218.
- Gagneur A, Dirson E, Audebert S, Vallet S. Materno-fetal transmission of human coronaviruses: a prospective pilot study. *Eur J Clin Microbiol Infect Dis* 2008; **2005**: 863–866.

22. Yudin M, Steele D, Sgro M, Read S, Kopplin P, Gough K. Severe acute respiratory syndrome in pregnancy. *Obstet Gynecol* 2005; 105: 124–127.
23. Bottomley C, Van Belle V, Pexsters A, Papageorghiou AT, Mukri F, Kirk E, Van Huffel S, Timmerman D, Bourne T. A model and scoring system to predict outcome of intrauterine pregnancies of uncertain viability. *Ultrasound Obstet Gynecol* 2011; 37: 588–595.
24. Bignardi T, Condous G, Kirk E, Van Calsters B, Van Huffel S, Timmerman D, Bourne T. Viability of intrauterine pregnancy in women with pregnancy of unknown location: prediction using human chorionic gonadotropin ratio vs. progesterone. *Ultrasound Obstet Gynecol* 2010; 35: 656–661.
25. Wang L, Shi Y, Xiao T, Fu J, Feng X, Mu D, Feng Q, Hei M, Hu X, Li Z, Lu G, Tang Z, Wang Y, Wang C, Xia S, *et al.*; Working Committee on Perinatal and Neonatal Management for the Prevention and Control of the 2019 Novel Coronavirus Infection. Chinese expert consensus on the perinatal and neonatal management for the prevention and control of the 2019 novel coronavirus infection (First edition). *Ann Transl Med* 2020; 8: 1–8.
26. Poon LC, Yang H, Lee JCS, Copel JA, Leung TY, Zhang Y, Chen D, Prefumo F. ISUOG Interim Guidance on 2019 novel coronavirus infection during pregnancy and puerperium: information for healthcare professionals. *Ultrasound Obstet Gynecol* 2020; 55: 700–708.
27. Centers for Disease Control and Prevention. Interim Considerations for Infection Prevention and Control of Coronavirus Disease 2019 (COVID-19) in Inpatient Obstetric Healthcare Settings, 2020. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/inpatient-obstetric-healthcare-guidance.html>
28. British National Formulary. Kaletra. <https://bnf.nice.org.uk/medicinal-forms/lopinavir-with-ritonavir.html>
29. British National Formulary. Chloroquine. <https://bnf.nice.org.uk/drug/chloroquine.html#indicationsAndDoses>
30. Mulangu S, Dodd L, Davey R, Mbaya O, Proschan M, Mukadi D, Lusakibanza Manzo M, Nzolo D, Tshomba Oloma A, Ibanda A, Ali R, Coulibaly S, Levine AC, Grais R, Diaz J, Lane HC, *et al.*; PALM Consortium Study Team. A Randomized, Controlled Trial of Ebola Virus Disease Therapeutics. *NEJM* 2019; 381: 2293–2203.

SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:



Appendix S1 Search strategy