

**Case Series**

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**Covid-19 in pregnancy: A case series of complexities and challenges in management, pregnancy outcome and review of literature at Northampton General Hospital UK**

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**Abstract**

**Objectives:** To describe the complexities and challenges in managing very complex and fascinating cases of Covid-19 in pregnancy at a district hospital in the UK.

**Case presentation**

**Case 1:** A 44-year-old African lady, G6P0+5 dichorionic diamniotic IVF twins, BMI 28kg/m<sup>2</sup>, complex medical history (essential hypertension, non-functioning pituitary macro-adenoma, partial hypopituitarism leading to diabetes insipidus, hypothyroidism, low cortisol, previous myomectomy, laparoscopies, hysteroscopies and endometriosis, gestational diabetes) was admitted at 32 weeks with features of Covid-19. She was confirmed Covid-19 positive but self-discharged, and eight days later, presented with confirmed Covid-19 pneumonitis. She was managed accordingly, but she had a caesarean section at 32 weeks due to worsening maternal condition and made a good postoperative recovery.

**Case 2:** A 35-year-old G1P0, BMI 31.6 kg/m<sup>2</sup>, gestational diabetic, presented at 34 weeks with worsening cough and breathlessness and was confirmed Covid-19 positive. Two days following admission, her condition worsened, and she had an emergency caesarean section. She deteriorated further in the postpartum period and was admitted to the intensive care unit (ICU), intubated and ventilated for an extensive period. She suffered multiple complications during her stay, including pulmonary embolism, bilateral pneumothorax, median nerve damage with residual left-hand weakness, rectus sheath haematoma, post-traumatic stress disorder (PTSD) and lung fibrosis. She was discharged home after more than a hundred day stay in ICU.

**Conclusion:** Covid-19 has impacted health care, and economies and these reports further elucidate its repercussions in pregnancy. There was, however, no mother to child transmission.

**Keywords:** SARS-CoV2; Coronavirus; Covid-19; Pregnancy.

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## Introduction

Covid-19, also known as SARS-CoV2 - severe acute respiratory syndrome coronavirus, has revolutionized medical practice, especially in treatment and prevention. Its effect has resonated in all specialities, including obstetrics and gynaecology. Discovered first in the Hubei province in Wuhan, China, in December 2019, its spread has been astronomical, with heightened morbidities and mortality across all age group around the globe [1, 2]. The World Health Organization (WHO), in their latest weekly report, confirmed a total number of 30,055,710 cases and 943,433 deaths at the time of writing this article [3]. In pregnancy, not much is understood as the disease is novel. Much of the published work is based on case reports, systematic reviews and meta-analysis of the available studies since the outbreak. According to the centre for disease control (CDC), since the outbreak, there have been 21573 cases of Covid-19 in pregnancy, with 48 deaths in the United States of America (USA) [4]. In the UK, according to the United Kingdom Obstetric Surveillance System (UKOSS) first report, there has been 427 cases (4.9 in 1000) of Covid-19 amongst pregnant women who were admitted to the hospital with five deaths [5,6]. In this case series, we report the prevalence of SARS-CoV-2 in pregnant women admitted to our maternity unit between March 2020 and August 2020 and present a case series of the number of coronavirus cases in the hospital at the time of writing this paper. We also present two complex and challenging cases of Covid-19 in pregnancy, where one of them spent over 100 days in the intensive care unit (ICU).

## Case 1

This was a 44-year-old African lady, G6P0+5, body mass index (BMI) 28 kg/m<sup>2</sup> with a dichorionic diamniotic (DCDA) twin pregnancy by in-vitro fertilisation (IVF) with donor egg and sperm. She booked at 12 weeks' gestation. Antenatal investigations revealed anaemia in pregnancy, gestational diabetes, and group B streptococcus (GBS) positive status. Her dating and anomaly scans showed multiple fibroids throughout the uterus with a fibroid located near the cervix measuring 43 x 40 mm with two fibroids noted in the lower segment, one in the anterior wall measuring 33 x 36 one in the posterior wall measuring 36 x 31 mm. Her venous thromboembolism risk core (VTE) was 3 (age, IVF and multiple pregnancy). She had five previous first trimester miscarriages. The past medical history revealed multiple comorbidities, including essential hypertension, non-functioning pituitary macro-adenoma previously operated, partial hypopituitarism leading to diabetes insipidus and low cortisol, previous myomectomy, laparoscopies, hysteroscopies and endometriosis.

She was on hydrocortisone, fluoxetine, ferrous fumarate, ranitidine, cabergoline and gabapentin (stopped when she got pregnant). She was allergic to quinine and zolmitriptan. She had a family history of tuberculosis, diabetes and hypertension and also suffered from depression and anxiety. The pregnancy issues were discussed with her, and she was managed in a multi-disciplinary clinic with an endocrinologist in Northampton General Hospital (NGH) and in Oxford and obstetricians. She was commenced on Aspirin from 12 weeks gestation, serial growth scans from 24 weeks and low molecular weight heparin from 28 weeks. At 16 weeks, she was started on insulin for gestational

diabetes. She was also commenced on levothyroxine for hypothyroidism and hydrocortisone.

Serial growth scans revealed tailing growth for twin two, and she was on continued foetal medicine surveillance.

At 31 weeks, she presented at the maternity day assessment unit (MDU) with cough and central chest pain. The observation was normal with a respiratory rate (RR) of 32 cycles per minute (CPM), heart rate (HR) 82 beats per minute (bpm), Blood pressure (BP) 158/86 mmHg, temperature (T) 36.9 degrees centigrade, and oxygen saturation (SpO<sub>2</sub>) was 97%.

She had a normal chest examination and normal cardiac examination. She was managed for Viral chest infection and was kept isolated because of high risk for Covid-19 and had a Covid-19 swab and other investigations. She had a normal electrocardiogram (ECG), cardiotocograph (CTG), chest X-ray, full blood count (FBC), C-reactive protein (CRP) and sputum microscopy, culture and sensitivity. Her Covid-19 swab was positive. She was admitted and received supportive care-thromboembolic stockings (TEDs), low molecular weight heparin (LMWH), analgesia, and antenatal medications. After a day of hospital stay, she requested discharge against medical advice. Implications of Covid-19 were discussed with her and advised to self-isolate for 14 days. Antenatal care (ANC) appointment rescheduling was done, and she was told to come in if short of breath or symptoms worsened. A week after discharged, she presented at Accident and Emergency with haemoptysis and shortness of breath. The observation was HR, 90bpm, BP 134/74 mmHg, T 36.5 degrees centigrade, RR 32 cpm, oxygen saturation was 93% on room air and required 4L of oxygen. Cardiotocography was normal. On physical examination, the patient looked well in herself. Her chest was clinically clear. Palpation of the abdomen revealed a soft abdomen with minimal suprapubic tenderness.

For investigations, FBC showed a reduced lymphocyte count of 0.75 (with a normal white cell count). A chest X-ray showed bilateral patchy ground-glass consolidations consistent with Covid-19. She was started on 2 L/min oxygen (O<sub>2</sub>) via nasal prongs and administered intravenous (IV) amoxicillin 1 g. She had a computerised tomography pulmonary angiography (CTPA) which showed no evidence of pulmonary embolism but multiple areas of ill-defined foci of airspace opacification with air bronchospasm and multiple ill-defined areas of ground-glass opacification diffusely distributed in both lungs. These changes were in keeping with Covid-19 bilateral pneumonia. A mid-left pleural effusion was also noted.

With worsening symptoms and increased oxygen requirement, she was planned for an emergency caesarean section after a course of corticosteroids for foetal lung maturity. Caesarean section was uneventful, and both babies were admitted into the special care baby unit in good condition. Her postoperative period was uneventful, and she was otherwise stable with an oxygen saturation of 95% on 3 L/min oxygen via nasal prongs and oxygen levels improved with decrease requirements. She was later discharged on day three postpartum. The babies were also subsequently discharged from special care and are doing well. The summary of the patient journey for case 1 is shown below.

## Case 2

A 35-year-old lady G1P0 34 weeks, BMI 31.6 kg/m<sup>2</sup> and was initially low-risk pregnancy. She booked at 12 weeks and had a normal dating scan and normal booking investigations. For the past medical history, she has had an appendicectomy. Drug and family history were not relevant, and for the social history, she was a factory worker, ex-smoker (stopped after conception), and had good support at home. At 13 weeks, she presented at the early pregnancy unit with vaginal bleeding and had a normal transvaginal scan and discharged after that. An anomaly scan at 20 weeks revealed a discrepancy in the size of the great vessels and referred to John Ratcliffe Hospital (JRH) Oxford. At JRH, she had a scan at 21 weeks which showed moderate pulmonary stenosis and was followed at 28 weeks. At 28 weeks, a further scan did not reveal additional anomalies. She was offered amniocentesis but declined it.

At 29 weeks, she was diagnosed with gestational diabetes. A growth scan at 31 weeks showed normal growth with normal liquor volume and dopplers. At 33 weeks, foetal cardiac assessment at JRH still revealed moderate pulmonary valve stenosis unlikely to require prostaglandin at birth; however, an early post-natal cardiac assessment was recommended. At 34 weeks +1 day, she presented at the maternity day unit (MDU) with a 3-day history of headache and reported about possible raised temperature when asked about Covid-19 symptoms. She had normal observations and was discharged on oral antibiotics.

At 34+5 days, she called the maternity day unit and reported a new-onset cough but no fever. She was advised to continue oral antibiotics and call back if symptoms worsen or she becomes unwell. At 35 weeks' gestation, she was admitted under medics with a 4-day history of cough and shortness of breath and was confirmed Covid-19 positive. The next day she had increased O<sub>2</sub> requirements, and continuous positive airway pressure therapy (CPAP) was commenced.

Two days following admission at 35 weeks +3 days, it was decided by the multidisciplinary team (MDT) of obstetricians, midwifery, anaesthetics, medical and paediatricians to deliver the baby by caesarean section under spinal and with special COVID-19 precaution. This was due to increased oxygen requirement and worsening maternal condition. Delivery was initially planned for Oxford, but it was decided for Northampton and ex-utero transfer to Oxford because of her condition.

She subsequently had an uncomplicated emergency caesarean section (EMCS) after a course of corticosteroids for foetal lung maturity. The baby was admitted to the neonatal unit and later transferred to Oxford. In the immediate postoperative period, her condition remained unchanged, although she was still on CPAP. She remained for five days in the medical ward on CPAP with obstetric input.

On day six postpartum, she was admitted to the intensive care unit (ICU) and intubated and ventilated. Her stay was prolonged and complex, requiring inotropes and chromotropes, dexamethasone and other medication with supportive care while still intubated and ventilated for more than eight weeks.

On day 64 of admission to ICU, while still being intubated and ventilated, she was diagnosed with pulmonary embolism and was commenced on non-vitamin K antagonist oral anti-coagulants (NOAC). She also developed postoperative wound infection and was treated with a prolonged course of antifungals and antibiotics and also developed median nerve damage

with residual left-hand weakness and had physiotherapy. She also had rectus sheath haematoma, and this resolved gradually during admission. Computerized tomography pulmonary angiogram (CTPA) during the prolonged stay revealed severe lung fibrosis, and there were discussions regarding lung transplantation. Royal Brompton advised it was not needed in the immediate term but maybe a future possibility. She was managed for Covid-19 pneumonitis with antibiotics and other supportive care amidst other complications of prolonged hospital stay and remained ventilated in ICU for 66 days. Results of imaging are displayed in figure 2 below.

On day 67 of her admission to ICU, she was extubated and had a tracheostomy removed on day 94. She also developed recurrent bilateral pneumothorax, and numerous chest drains were inserted, and she remained in ICU requiring oxygen. She had ongoing rehabilitation and dietician support and daily dressing of caesarean section wound. She also had specialist perinatal mental health service support for post-traumatic stress disorder and anxiety. Her oxygen requirement gradually reduced, and she was maintaining her saturation at 97% in room air.

She made a remarkable recovery, and on day 108, she left ICU and was transferred to the medical ward; on day 110, she was discharged with a standing ovation on the corridor with all the staff involved in her care. She has been subsequently followed up with no concerns, and the baby was also doing well at Oxford.

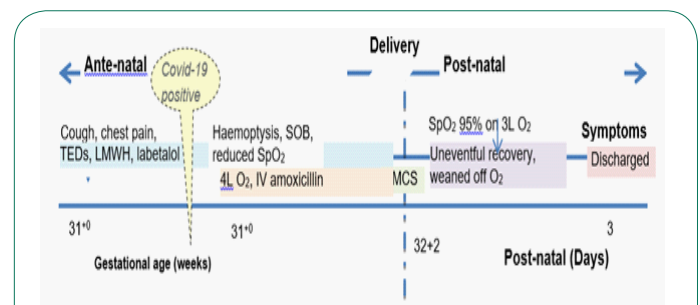


Figure 1: Summary of patient journey for case 1.

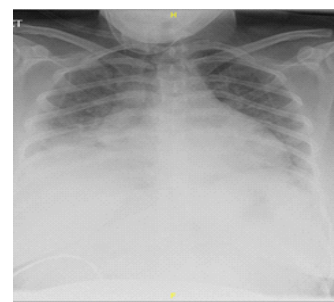


Figure 1A: Chest radiograph in keeping with Covid-19 pneumonitis.

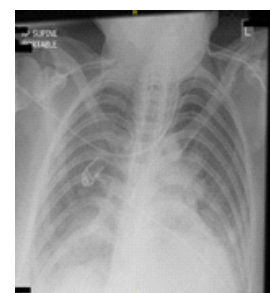
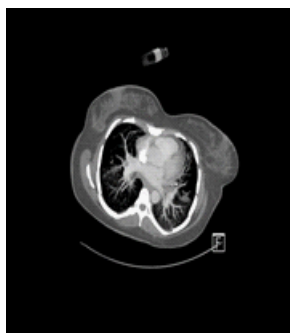


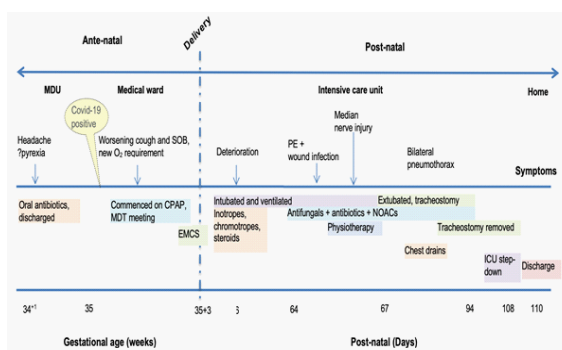
Figure 1B: Patient improving but chest XRAY in keeping with Covid-19 pneumonitis.



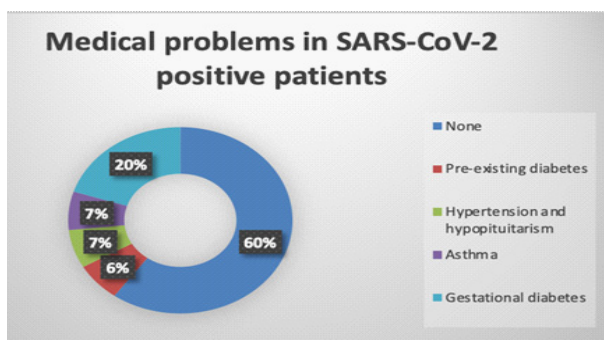
**Figure 1C:** CTPA showing extensive and diffuse ground glass opacification involving both lungs with relative sparing of the apical segments. Interspersed areas of focal consolidations are also seen in the bases and pulmonary thromboembolism in the middle lobe segmental artery.



**Figure 2:** Chest X-ray and CTPA showing Covid-19 pneumonitis and pulmonary embolism.



**Figure 3:** Summary of patient journey for case 2.



**Figure 4:** Record of Covid-19 patients and medical problems.

**Table 1:** Record of Covid-19 patients and medical problems.

	Ethnicity	Age (years)	Symptomatic of covid-19	Booking BMI (Kg/M <sup>2</sup> )	Pre-existing medical problems	Pregnancy complications
1	Asian	32	Yes	21.6	No	Gestational diabetes at 28/40
2	White European	35	Yes	31.6	No	Gestational diabetes at 28/40
3	White European	27	Yes	27.6	No	Gestational diabetes at 28/40
4	White British	30	No	19.7	No	No
5	White European	37	No	28.3	No	No
6	Black African	38	No	32	No	No
7	White British	26	No	30.1	No	No
8	Black African	45	Yes	27.6	Essential hypertension	Twin pregnancy
9	White British	25	No	24.3	No	No
10	Chinese	32	No	19.1	No	No
11	White European	32	No	22.2	No	No
12	White European	23	No	16	No	No
13	White British	32	No	31.4	Pre-existing diabetes	No
14	White European	24	No	21.9	No	No
15	White British	24	No	37.6	Asthma	No

### Discussion

Coronavirus disease (Covid-19) is one of the phenomena that has hit the 21st century like a thunderbolt claiming lives in a similar fashion and proportion as the 20th-century Spanish flu. Not much is known about the behaviour of this novel disease, and it remains an enigma that is constantly unfolding. Currently, there is no evidence that pregnant women are more susceptible compared to the general population [7-9]. Regarding foetal-maternal transmission, evidence suggests the slightest possibility of this, although more robust work is needed to further establish this claim. Furthermore, reports have shown the evidence of immunoglobulin M (IgM) for Covid-19 in neonatal serum and high placental viral load, and the UKOSS report also corroborated this [5,6,10]. On the contrary, other reports and systematic reviews have not found any evidence of mother to child transmission [2,11-16]. In this report, we present two interesting, complex and very challenging cases of our obstetric patients who were caught in the web of the virus just as it was making waves in the UK. This report looked at the total number of Covid-19 pregnant patients since the outbreak, and there were 15 of them. Of the 15, 11 were asymptomatic (73.3%), 3 had pre-existing medical conditions (20%), and 3 had gestational diabetes diagnosed (20%). This is shown in table 1 and figure 4. Three of the patients with diabetes were symptomatic with fever and cough with no respiratory difficulty. They all self-isolated and made a good recovery.

Case 1 presents a 44-year-old lady, IVF pregnancy with a complex medical history who was shielding and later contracted the virus in the third trimester. With increasing oxygen requirement and deterioration in health, she had an EMCS at 32 weeks for maternal condition. Case 2 presents a 35-year-old lady who caught the virus at 35 weeks gestation and had emergency delivery for worsening maternal condition. She was admitted to ICU and remained there for over 100 days.

Some of the risk factors associated with coronavirus disease are age greater than 35 years, ethnicity, commodities, and vitamin D deficiency [1,5]. The UKOSS survey disclosed that pregnant women of black and ethnic minorities women with commodities and obese women were more likely to be admitted into the hospital with covid-19 [6]. Commodities and risk factors noted in the first case presentation were race, age, essential hypertension, panhypopituitarism (hypothyroidism) as well as gestational diabetes. For the second case, the risk factors and commodities were age, BMI of  $>30 \text{ Kg/m}^2$  and gestational diabetes. These may have contributed to the acquisition and severity of Covid-19 in these women as they have been associated with Covid-19 in pregnancy with particular reference to diabetes (gestational or pre-existing) [6,17]. Asma Khalil and colleagues, in their systematic review and metanalysis, found that women of black, Asian or minority ethnic origin (BAME) who were known to be susceptible to the disease were 50.8% and 38%. Of these women, obesity and asthma were the comorbidities in 32.5%. These findings were all statistically significant [18]. Also, a systematic review and metanalysis of 77 studies by John Allotey and associates concluded that the risk of Covid-19 was increased with women with advanced maternal age, pre-existing commodities and high BMI [19]. These risk factors and comorbidities have also been corroborated by other studies and reviews [20].

Specific pregnancy outcomes have been reported in patients with Covid-19. These include increased risk for miscarriages, stillbirth, preterm labour and delivery, growth restriction, need for caesarean delivery, intensive care admission/intubation, and disseminated intravascular coagulopathy [7,12,18,19,21,22]. There is still limited evidence on the increased risk of miscarriages and intrauterine growth restriction (IUGR) [1,14].

Symptoms in pregnancy usually vary from mild to severe, with hypoxia suggestive of Covid-19 pneumonitis. This is particularly marked in a patient with immunosuppression and commodities [5]. John Allotey and associates revealed that pregnant women with Covid-19 were more likely to have preterm labour than their non-pregnant counterparts [19].

The UKOSS report on the review of 427 women with Covid-19 in pregnancy revealed that the average gestational age for hospital admission was 34 weeks, and approximately 50% of them had a caesarean section for foetal-maternal compromise, three of the women required level 3 care and four received extracorporeal membrane oxygen (ECMO) with 5 deaths. The cause of death is still unclear [6]. Also, the weekly report of the United Kingdom intensive Care national audit and research centre (IC-NARC) revealed that of the 10,834 intensive care admissions, 63 of them were pregnant women [23]. The literature is replete with case reports of various pregnancy outcome and lengths of stay in the ICU due to Covid-19, and further work is needed on the short and long term implications of Covid-19 in pregnancy.

Foetal outcomes reported include IUGR, preterm births admission into neonatal intensive care unit (NICU) and perinatal

deaths [1]. More studies are also required to elucidate these associations further. Regarding breastfeeding, there is limited evidence to suggest the presence of coronavirus in breastmilk [15]. Management in pregnancy requires an initial assessment of the patients with triaging into inpatient and outpatient treatment depending on their clinical presentation. Symptoms assessed include fever, shortness of breath (SOB), cough, pharyngitis, rhinorrhea, ageusia or anosmia. Clinical investigation of relevance consists of a full blood count (FBC), electrolyte, urea and creatinine (U&E) LFT, chest-Xray, and chest computerised tomography (CT). Results consistent with Covid-19 include lymphopenia, raised CRP, thrombocytopenia (mild), increased liver function and creatine phosphate [24,25]. The cases presented had the relevant diagnostic laboratory and radiological features of severe disease. Although real-time polymerase chain reaction (PCR) is the goal standard for diagnosing Covid-19, chest CT has a greater sensitivity than RT-PCR (98% versus 71%) [25,26].

Patients with symptoms or suspected to have Covid-19 can self-refer for testing. Those with a mild (symptomatic but with stable clinically) disease confirmed to have Covid-19 can be managed on an outpatient basis by self-isolation and observing public health measures to curtail its spread and pregnancy managed according to standards in Royal College of Obstetricians and Gynaecology (RCOG) guidelines. This also applies to asymptomatic women [5].

Patients with severe disease evidenced by SOB with  $\text{RR}>22\text{cpm}$ ,  $\text{T}>37.8$  degrees, oxygen saturation  $\leq 93\%$ , comorbidities and respiratory failure or end-organ damage should be admitted and cared for by a multidisciplinary team adorned in appropriate personal protective equipment (PPEs). The team consist of obstetricians, midwives, anaesthetics, physicians and intensivists [25].

Initial management is supportive with oxygen therapy, hydration, monitoring of oxygen saturation, and electrolytes. Specific treatments employed include antiviral, antibacterial, corticosteroid (dexamethasone). Betamethasone can also be given for foetal lung maturity when needed. Admission into ICU may be indicated, and patients may require intubation, mechanical ventilation or ECMO [25].

Pregnancy poses challenges in the management of Covid-19 since symptoms of Covid-19, such as SOB, is similar to the cardiorespiratory changes in pregnancy. Also, considerations are given to the foetal-maternal wellbeing as we weigh the risk of prematurity and early delivery against the maternal condition. The second patient had a very severe disease requiring delivery at 35 weeks to improve maternal pulmonary function. This was challenging to weigh the balance between delivery and prematurity.

#### **Challenges faced with the 2 cases were:**

1. Managing deteriorating maternal status, including morbidities associated with a prolonged hospital stay, prolonged ICU stay and long-term effect of oxygen therapy on the lungs (fibrosis).
2. Early delivery and balancing this with problems of prematurity.
3. Mode delivery (caesarean section) with the logistic challenges of needed staffing, the timing of delivery, personal protective equipment (PPE), intubation with the generation of aerosol and postoperative care.

### 3. Separation of the baby from mother.

Delivery usually depends on foetal-maternal condition as well as obstetric indications. Usually, the caesarean section has been the preferred route in over 90% of cases in hospitalised pregnant women to improve maternal respiratory status [25]. Preterm delivery has been noted to be the most adverse outcome in pregnancy. Both patients in this review were delivered preterm [27].

Postoperative care involves the standard care for all women in addition to thromboprophylaxis, continuing dexamethasone, oxygen saturation monitoring and supportive care. Patients who make remarkable recovery are discharged early to limit the spread of the virus and protect other patients and staff.

#### Future research

Going forwards, randomised controlled trials (RCTs) are needed to clarify the effectiveness and safety of existing therapies, the chances of maternal and child transmission and also shed more light on the behaviour of this novel disease in pregnancy. There seems to be a glimmer of hope with the approval and use of the Pfizer-BioNTech, Oxford University AstraZenika and Moderna Covid-19 vaccines to prevent the disease [28]. Little or nothing is known about their safety in pregnancy, and further research is required for clarity.

#### Conclusion

Covid-19 has impacted health care and economies with huge implications. This case report and review further elucidate the impact of this disease in pregnancy with women who had multiple commodities and the adverse pregnancy outcome of preterm delivery and problems of prematurity. Standards of care and treatment as outlined by WHO and RCOG must be followed. Curbing its deadly spread still requires the concerted efforts of social distancing, face coverings, effective handwashing at least for 20 seconds and limiting contact with potential carriers and high-risk individuals.

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