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Case Report

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Innovative mid-trimester termination of pregnancy in a COVID-19 critically Ill patient

Abstract

The current COVID-19 pandemic has introduced many challenges on the presentation of the disease, effects of the disease on co-morbidities of the patient and the management of these. This has necessitated innovative ways of managing these patients. This is particularly so in pregnant women with COVID-19.

We present a case of a pregnant woman in her mid-trimester who presented with severe COVID-19 disease requiring ICU admission who required termination of pregnancy due to worsening condition while on ventilator. She presented with high fever, cough and difficulty in breathing. These rapidly deteriorated requiring ECMO. Her liver function, kidney function and inflammatory markers equally deteriorated very fast despite various treatments including using convalescence plasma. We decided to terminate the pregnancy to help in managing her condition. The baby died just when we were considering the termination of the pregnancy thus requiring Mid-trimester termination of the non-viable pregnancy. We initially tried to use vaginal misoprostol for the termination but failed thus we had to find a way of using mifepristone pre-treatment for the termination. An innovative used of mifepristone through the nasogastric tube was devised and we successfully terminated the pregnancy with mifepristone pre-treatment followed by a single dose of misoprostol with minimal blood loss. The patient's condition improved rapidly after the termination of pregnancy and she recovered fully. We feel her pregnant status might have contributed to her severe symptoms and the disease may have contributed to the demised of the baby. We recommend the use of mifepristone through the nasogastric tube in the process of termination of pregnancy in a sick ventilated patient.

Keywords: pregnancy, challenges, COVID-19, innovative, mid-trimester, termination, mifepristone, nasogastric

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Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BP, blood pressure; COVID, corona virus disease; CRP, C-reactive protein; ICU, intensive care unit; IV, intravenous; MDT, multi-disciplinary meeting; NG, nasogastric; PCR, polymerase chain reaction; RT, reverse transcription; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

Background

The advent of COVID-19 (novel coronavirus disease 2019) and its declaration as a global pandemic has forced us to make many changes in the way we do things throughout the world.[1,2] This is particularly so in the medical profession. In addition, patients with COVID-19, particularly those with severe disease requiring ventilation, pose a challenge not only in managing their disease, but also how to manage their co-morbidities; Thus the need for innovative solutions. The management of COVID-19 patients who are pregnant present such challenge in providing antenatal care, termination of pregnancy, labour, delivery and postpartum care for these patients. We faced the challenge of mid-trimester termination of pregnancy in a ventilated patient in intensive care unit (ICU), who has COVID-19. Mid-trimester termination of pregnancy in itself poses some problems as despite the fact that such cases account for 10-15% of induced abortion, they account for two-third of major complications of induced abortions. Mid-trimester termination of pregnancy in a patient on ventilation with severe COVID-19, as in our case, therefore creates major risks and difficulties.

The introduction of Mifepristone (RU486) in mid-trimester medical termination of pregnancy, where foetal survival is not a major issue, within the last two decades has improved patients management. The combination of mifepristone (pre-treatment) and prostaglandins is now a well-established method of mid-trimester termination of pregnancy.[3–5] Mifepristone is synthetic steroid that has an anti-progestin effect by competitively blocking the progesterone receptors.[6–16] Normally mifepristone is administered orally,[14–16] thus making its use in an ICU ventilated, especially COVID-19,patient a challenge. Finding a way to administer this drug will be a valuable addition to successfully manage ventilated patient, especially in COVID-19 cases.

With the Covid-19 pandemic continuing and the disease actively spreading throughout the World with second and third waves in many countries who had the disease for over a year now,[17] it is important continue to share our experience on the manifestation and perinatal outcome of pregnant women with Covid-19. In addition, the innovative administration of mifepristone need to be shared to help in the management of such patients on ventilation. We present a case of a young woman with severe COVID-19 in mid-trimester of pregnancy who was on ventilation and required mid-trimester termination of pregnancy. We used novel route of administering mifepristone, in combination with vaginal misoprostol to terminate the pregnancy. We terminated the pregnancy successfully with this combination after vaginal misoprostol alone failed. The initial use of vaginal misoprostol alone without pre-treatment with mifepristone was because of doubt

about its route of administration. The patient improved significantly after the termination.

Case report

Our patient is a 38 year old, Gravida 2, Para 1 lady who presented to our emergency at 23 weeks and 3 days gestation with fever and productive cough for 7 days and shortness of breath with fatigue for 2 days. Her shortness of breath and fatigue got worse within the last 24 hours before presentation. She had no recent history of travel or contact with a sick patient and had no history of any medical or surgical illness. In particular, she had no asthma, diabetes, hypertension or any cardiovascular disease. On examination, she was breathless and her vital signs were; BP 145/86mmHg, pulse 113/min, RR 28/min, temperature 37.5 degrees Celsius and oxygen saturation was 89% on 3 litres of oxygen. Uterine fundal height was equivalent to 24 weeks gestation with normal foetal heartbeat. There was no uterine contraction or tenderness and no vaginal bleeding or discharges.

She was admitted to the medical ICU as a suspected case of COVID-19, after initial investigations including nasopharyngeal and oropharyngeal swabs for RT-PCR for SARS-CoV-2 was taken and chest X-ray done. Chest X-ray revealed bilateral basal lung consolidation with interstitial shadowing, prominent bronco-vascular marking and diffuse peri-hilar feature suggestive of viral pathology. She was, immediately, started on Tazocin and oseltamivir based on the presentation and the X-ray findings. The liver and kidney function tests were essentially normal, as was the coagulation profile. The haemoglobin (Hb) was 11.4gm/dl, White blood cells (WBC) 13.7 x10/L and platelets 345 x10/L with lactic acid of 1.4mmol/L and D Dimer of 0.97mg/L. The swabs confirmed positive SARS-CoV-2 infection. Ultrasound scan at this stage showed a 23+ weeks foetus with normal heartbeat and biometry.

Her breathing deteriorated rapidly and she was intubated 12 hour after her presentation. Her medications were changed to intravenous azithromycin, hydroxychloroquine NG, lopinavir/ritonavir NG, tocilizumab IV and Tazocin was continued. The patient condition was not improving therefore she had to be placed on inotropes to stabilise her vital signs. She was started on convalescent plasma therapy on the second day of her admission.

Patient's, arterial oxygen partial pressure/fractional inspired oxygen (P/F)ratio deteriorated further and she was placed on Extracorporeal membrane oxygenation(ECMO) 6 days after her admission. Her Hb then was 9.7gm/dl but this dropped to 8.3gm/dl the following day. Platelets count and coagulation profile were normal. There was no vaginal bleeding and abdominal ultrasound scan showed normal placenta and foetus with no collection or haemtoma. Her haemoglobin continued to drop and she had repeated blood transfusion. Subsequent imaging showed abdominal wall haematoma of about 18.5x16.5x10.5cm in size but coagulation profile remained normal at that stage. That haematoma was considered to be from the ECMO procedure. The haematoma did gradually subside without any surgical/radiological intervention.

Her liver function tests (LFT) started deteriorating from the fifth day of admission and the ALT reached 612units/L and AST of 324units/L. Antiretroviral drugs had to be stopped on the 9th day of admission(8th day of antiretroviral combination administration).These improved and normalized within a week.

Her serum urea rose to 9.1mmol/L on the 3rd day after admission but the creatinine was normal until the 11th day when the creatinine reached 112micmol/L and urea was 21.1mmol/L. These rapidly deteriorated to urea of 34.9mmol/L and creatinine of 165micmol/L within the following 2 days with compounded oliguria. In view of the worsening renal function, the patient was started on renal dialysis. There was deteriorating renal function (probable acute kidney injury), rising liver enzymes, haemoglobin 6.4gm/dl (dropped despite repeated blood transfusion), WBC 50, CRP 60mg/dl (worsen to 250mg/dl during induction process). At this stage, the patient was requiring inotropes and oxygen saturation remained poor despite ECMO but foetal heartbeat was still present. In view of these, we held an MDT meeting. At the meeting, we reached a decision to terminate the pregnancy to help in the management of the mother. This was 13 days after admission, at 25+-week gestation. Foetal heartbeat was checked, on the day of delivery, and found to be absent and intrauterine foetal death (IUFD) confirmed by ultrasound scan, thus we proceeded for mid-trimester termination.

At the start of termination, the cervix was posterior, long and firm with a closed cervicalos. Termination of the pregnancy was started using Misoprostol 200mcg vaginally every4 hours as per our protocol. There was no cervical change after a full course of misoprostol. At that stage, we decided to use the combination of mifepristone and vaginal misoprostol. To overcome the challenge of administering the mifepristone we decided to administer it through the nasogastric (NG) tube.

We crushed the mifepristone and administered it through the NG tube. About 19 hours after the mifepristone vaginal examination was done to insert misoprostol. At this stage, the cervix was still posterior but 2cm dilated, thus Misoprostol 200mcg was inserted at the posterior vaginal fornix at this stage. The patient delivered the foetus together with the placenta within one hour of this last misoprostol insertion. There was only 200mls of blood loss and subsequent lochia was normal throughout. The patient's condition dramatically improved. Her oxygen saturation improved from 90% to 97% within 30 minutes and 99-100% after 3 hours. The following day, after the delivery her, her WBC and CRP were down to 30.9 and 27.1 respectively.

She continued to make good steady progress and ECMO was de-cannulated three days after the delivery. She was weaned off the ventilator gradually and was extubated on the sixth day after delivery. The surgical team managed the muscular haematoma conservatively. It resolved gradually with the haemoglobin remaining stable at 8.7gm/dl and finally 10.6gm/dl without the need for further blood transfusion.

Discussion

The clinical presentation and impact of COVID-19 in different patients groups are still emerging as the disease continues to affect all strata of society all over the world. This is particularly the case with COVID-19 in pregnancy. Earlier data on the presentation, impact and management of this new disease (Covid-19) has been, mostly, from older non-pregnant patients (1). However, recent data shows that pregnant women are affected and seem to have more severe disease requiring hospitalization and ICU admission[17]. This and the recent waves of increase infections leading to second and third waves in many countries the discovery of mutated new viral types add more urgency to understand the presentation, effect and management of this disease in pregnant women.

There are few case reports on COVID-19 in the first and second trimester of pregnancy recently. Our case of severe COVID-19 in second trimester of pregnancy, therefore, provide important additional information on this disease in pregnancy. In addition our case bring in a new approach of administering mifepristone for termination

of pregnancy in very sick patients on ventilation and this add an important, possible, new way of managing COVID-19 patients on ventilation who require termination of pregnancy. Most reviews show Covid-19 in pregnancy is mostly seen in the third trimester. Sonja A. Rasmussen et al, in an earlier review of COVID-19 and pregnancy reported that there were only 18 cases of COVID-19 in pregnancy and all were infected in the third trimester (1)). In that review, the authors highlighted the need to collect and report information on COVID-19 in pregnancy. In a subsequent review comprising 108 infected pregnant patients, it was reported that all the patients presented in the third trimester of pregnancy (Jerome Bouaziz 14 May 20203). Liu reported 13 cases of pregnant women with COVID-19 out of which only two were less than 28 weeks of gestation.

Our patient presented in the second trimester of pregnancy thus making this an important addition to the body of emerging information. In a review, Bouaziz J reviewed 174 pregnant women with COVID-19 (from 23 case reports, case series and case control studies) and very few of these cases were in the second trimester of pregnancy.[3] The evidence from earlier reviews showed that clinical presentation of COVID-19 in pregnant women is similar to non-pregnant patients. In a review of 18 studies with 114 pregnant patient 87.5% had fever, 53.8% had cough, 22.5% had fatigue and 11.3% had had shortness of breath.[4]

Emerging recent data, however, showed that pregnant women seem to have more severe disease requiring hospitalization and ICU admission.[17] Our patient had fever, cough, shortness of breath and fatigue and had a severe disease requiring ICU admission. Preterm delivery and small for gestational age are the most common foetal adverse effects reported in pregnant patients with COVID-19. However, there are also few reports of stillbirth. In a WHO report, a review publication on 7th April 2020 involving 108 pregnant women, there was one intrauterine death. Also in a paper by Liu there was one stillbirth out of the 13 cases.[11] In another study, Della Gatta reported one stillbirth in a series of 48 cases who delivered.[12] Ziyi Yang et al also reported a 1.2% stillbirth in the 18 studies, comprising of 114 patients, that they reviewed.[4] In our case, we planned to terminate our patient's pregnancy for maternal reason but she had an IUFD just before the start of the delivery induction to terminate the pregnancy. This case therefore add to the number of IUFD in COVID-19 pregnant women.

At the early stages of the pandemic, most studies reported very few pregnant women with COVID-19 who develop severe disease. In a pooled data of 147 patients, the WHO reported 8% with severe disease and only 1% in critical condition and they suggested that pregnancy does not appear to be a risk factor for severe COVID-19 disease.[3] In another review of 114 cases in 18 studies, Ziyi Yang reported 6 cases (5.3%) with severe or critical disease which include one critical case with multiple organ failure requiring the use of ECMO[4]. However, recent data has clearly shown that pregnant women seem to have more severe disease requiring hospitalization and ICU admission. This may well be because of the various mutated new variant of the virus. Our patient had a severe disease and was in a critical condition with multiple organs (including liver and kidney) failure, and required ECMO for oxygenation. Many other publications reported multiple organs failure involving the liver, kidneys and respiratory system requiring ECMO.[2,6,10,11]

Reports have consistently shown that Caesarean section is the commonest route of delivery of patients with Covid-19 and it account for about 91% of all deliveries in this group of patients.[3,4] It seem delivering these patients; at any gestation pose a problem. Our patient required mid-trimester termination of pregnancy and this is usually a challenge even in non COVID-19 and non-intubated patients.[5] Recent developments using a combination of mifepristone and prostaglandin (misoprostol in particular) has improved the process of termination of pregnancy where the survival of the foetus is not a consideration. This combination therefore has become the best, effective and save method of mid-trimester termination of pregnancy.

However, there is paucity of any data in the literature for mid-trimester termination of pregnancy in COVID-19 patients. We could not find any report on mid-trimester termination of pregnancy in a patient with COVID-19 on ventilation. In addition, we could not find any report/data on the use of mifepristone through the nasogastric tube for termination of pregnancy. We believe our case is the first case of successful mid-trimester termination of pregnancy in a critically ill and ventilated COVID-19 patient using mifepristone pre-treatment. We equally believe that our case is the first report of using the NG tube to administer mifepristone. This novel idea of administering mifepristone through the NG tube, provide a new route of administering and, therefore, use of mifepristone in combination with vaginal prostaglandin to safely terminate pregnancies in ventilated patients. We could apply this for termination of pregnancy, at any stage of pregnancy, where survival of the foetus is not a consideration. Prostaglandin alone may fail to terminate pregnancy, in many cases, especially in mid-trimester of pregnancy. A combination of prostaglandin with mifepristone pre-treatment is usually more effective and safer. In our case, vaginal misoprostol alone failed but the combination of mifepristone pre-treatment through the NG tube and a follow up with a single dose of misoprostol successfully terminated the pregnancy within a short time and with only 200mls of blood loss and no other complications.

Conclusion

Our case add information on the presentation of COVID-19 in pregnancy, particularly at the early stages (mid-trimester) of pregnancy, and the possible impact of COVID-19 on the mother and foetus. We also believe that the novel administration of mifepristone through the NG tube give us a new route to consider in termination of pregnancy in ventilated patients, especially during this COVID-19 era. Despite this being just one case report, we hope that reporting the case improve our understanding and management of pregnant patients with COVID-19.We call on other clinicians to report more cases of COVID-19 in pregnancy at various gestational ages, detailing presentation, management and maternal and foetal outcome. We recommend the use of mifepristone through the NG tube in ventilated patients, in combination with vaginal prostaglandin for termination of pregnancy and urge clinicians to report their experience to validate this novel NG route of mifepristone administration.

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Conflicts of interest

Author declares that there is no conflict of interest.

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