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Spontaneous Abortion in Pregnancies Having COVID-19 Infection in Bangladesh: A Series of Cases

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Authors' contributions

This work was carried out in collaboration with the authors. Author TIC performed the medical advice and service of the patient and wrote the protocol, author TRC prepared the first draft, author MMR revised and edited the manuscript, authors NA and NAM performed the medical advices, author MJA final edit of English, Author TRD supervised the whole medical treatment and other activities. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Background: Coronavirus Disease (COVID-19) is a highly contagious disease and spreading all over the world. Pregnant women are particularly vulnerable to this infectious disease. There are not many reports on missed-abortion or stillbirths in COVID-19 that affected pregnant women.

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Twelve cases are presented here among a few cases of spontaneous abortion or fetal demise without having remarkable cause other than laboratory-confirmed COVID-19 (RT-PCR) from March 2020 to July 2020 in a single medical university hospital in Bangladesh.

Cases: Enrolled 12 pregnant subjects of fetal demise ≥11 weeks of gestation had COVID-19 infection (RT-PCR) and the specimen taken was nasal swab. 10 patients were admitted to the hospital and 2 patients were managed in their home under the supervision of Bangabandhu Sheikh Mujib Medical University (BSMMU). We excluded all the possible causes of clinical and obstetric causes of abortion other than COVID-19 infection. However, most of them were asymptomatic COVID-19 infection carriers, and only had a history of low-grade fever. 5 cases had a history of medical disorder which were controlled before pregnancy.

Conclusion: All the 12 cases did not have any clinical and obstetric disorder during pregnancy, but they all had COVID-19 infection. This suggests COVID-19 infection might induce fetal death through possible inflammation in the placenta.

Keywords: COVID-19; Pregnant women; abortion; case; RT-PCR.

1. INTRODUCTION

The coronavirus disease (COVID-19) is a serious Public Health Emergency and Global Crisis. It was declared a pandemic in the world by the World Health Organization (WHO) in March 2020. It transmits through respiratory droplets and a small airborne particles mainly and perinatal transmission is not well understood [1-3]. However, a previous report said pregnant women usually developed a mild form of COVID-19 despite a few cases for acute form with maternal morbidity and mortality [1,4-5]. A pregnant woman is immunologically weak and has a unique immunologic state where the maternal immune system tolerates paternally derived fetal antigens that lead to increase susceptibility to infection especially Pneumonia [3-6]. Physiological and Mechanical Changes enhance infection rate, especially Respiratory tract infection. Early pregnancy is a challenging and vulnerable period and affects embryogenesis and fetal organ development.

At present, there are limited resources for the guidance of the Critical Care Management of Pregnant patients with COVID-19 infection. Also, the miscarriages or fetal demises due to COVID-19 is not established yet due to very few reports on this particular issue [1, 7-10]. Thus, it is very important to have more evidence-based studies to establish the interrelationship between COVID-19 infection during pregnancy and the risk of miscarriages and fetal deaths for proposing suitable interventions.

Here, a case series is presented which included twelve cases of miss-abortion or fetal death in pregnant women having COVID-19 infection. To the best of our knowledge, this report is the first one in Bangladesh. All the patients were attending Gynecology Emergency and OUT PATIENT DEPARTMENT in Bangabandhu Sheikh Mujib Medical University (BSMMU) in Bangladesh and managed in this single institute from March 2020 to July 2020. All the fetal demise cases were ≥11 weeks of gestational age determined clinically with the help of the earliest Ultrasound (US) scan. Abortion was confirmed in the same way with laboratory-confirmed COVID-19 *via* Real-Time Polymerase Chain Reaction (RT PCR) assay of maternal nasal swab specimens. In this study, all the possible causes of abortion such as fetal malformations, placental abruption, placenta previa, preeclampsia, diabetes, auto-immune disorders, maternal trauma, etc. were excluded other than COVID-19 infection. This case series can be expanded that will help to acquire the knowledge in pregnancy along with a novel presentation of COVID-19 and hope this study will contribute to the pool of knowledge regarding COVID-19 infection in pregnancy to develop an intervention.

2. CASE SERIES

We enrolled 12 cases of fetal demise at 11 or more weeks of gestation with COVID-19 positive cases who were attended in the Gynecology Emergency and OUT PATIENT DEPARTMENT in the studied institute March 2020 to July 2020. The COVID-19 was confirmed by the laboratory (RT-PCR) from the nasal swab specimen. Ten patients were admitted to the hospital and two patients were managed in their home under the supervision of this institution. A total of 353 pregnancy cases were reported during the study period. Among them, about 16% was found missed-abortion. But we excluded all the

possible causes of clinical and obstetric causes of abortion other than COVID-19 only in 12 cases, which was selected for this case reporting. Among most of them were asymptomatic COVID-19 career, and only had a history of low-grade fever but no respiratory difficulties. So,they were diagnosed as mild Covid. Five patients had a History of Medical Disorder which was controlled before pregnancy. All the patients were successfully discharged from the hospital in afebrile condition. The patients were diagnosed as a case of missed-abortion by clinically and ultrasound scan (US).All the patients were attended in Gynaecological Emergency and OUT PATIENT DEPARTMENT. So, pre-pregnancy BMI were not available. Patient characteristics (age, gestational age, body mass index (BMI), and parity) are presented (Table 1).

2.1 Case 1

A 22 years Primi Gravida (G1 P0) patient was admitted to the hospital . She has a normal Body Mass Index (BMI) and no medical disorder was found.She attended in Out Patient Department at her 20 weeks of pregnancy with the complaint of prevaginal bleeding for one day. The patient having a history of low-grade fever 5 days ago but no other respiratory symptoms.On examination, she was found normotensive, heartbeats 100/min, and afebrile. Her initial investigation reports were normal in pregnancy, but at her 20 weeks of pregnancy, she did an ultrasonogram (US) and was diagnosed as a case of missed-abortion, and admitted to the hospital. Miscarriage was managed medically and an RT-PCR was done for potential COVID-19 infection and it turned out positive. Regarding the treatment of COVID-19 only symptomatic treatment was given. The patient was discharged and again test for COVID-19 was done 14 days after the initial diagnosis and found to be negative. So, the case was Diagnosed a 20 weeks missed-abortion with COVID-19 (Mild) positive. Fetal autopsy and placental histopathology were not done.

2.2 Case No-2

An obese woman of 26 years having 2nd Gravida and Para 1 (G2 P1) was treated in the gynecology emergency of the hospital. She was at her 21 weeks of pregnancy with lower abdominal pain but having no other medical disorder. During her examination, she was found normotensive, normal heartbeats, and afebrile. Her previous pregnancy report was normal. But this time the US was done with an outcome of a 20 weeks missed-abortion. The patient was admitted and abortion was managed by medical treatment and released after a few days. Later on, she was advised to do RT-PCR for COVID-19 infection confirmation and found to be positive. So, the case was diagnosed as a 21 weeks missed-abortion with COVID-19 (mild). The test was repeated after three weeks and was found Negative. Fetal autopsy and placental histopathology were not done.

2.3 Case No-3

Here, a 30 years old obese woman with 2nd Gravida and Para 1 (G2 P1) was attended to in the gynecology unit. She was at her 20-weeks of pregnancy having per vaginal bleeding and lower abdominal pain with a low-grade fever 4 days back before coming to the hospital. The patient has a history of bronchial asthma which is managed by a Salbutamol inhaler. She had no other medical disorder. However, on examination, she was found afebrile, normotensive, heartbeats of 102 /min, and symphysis fundal height-18 weeks. Her initial investigation reports were found clear and normal. During this visit, she was again examined with the US, and the report was found to be a 16-weeks missed-abortion. RT-PCR for COVID-19 was done and found to be positive. Abortion was managed by Medical treatment and discharged after 2 days. Again RT-PCR for COVID-19 was done after 14 days and found to be negative.

2.4 Case No-4

In this case, a 26 years old pregnant woman having 2nd Gravida and Para 1 (G2 P1) was reported in the gynecology unit of the hospital. She claimed a 14-weeks pregnancy with per vaginal bleeding for the last two days and she was obese. On a medical query, the patient gave the history of hypothyroidism controlled by drug tablet Thyrox (50 µg) daily. The patient had a history of the lower segment caesarian section (LSCS). She did not give any history of fever and any respiratory symptoms. However, on examination, she was afebrile, normotensive, and heartbeats 90 /min. On per vaginal examination, bleeding present, and OS-closed.

Her initial investigation reports were normal. However, a 14-weeks missed-abortion was found through the US. Abortion was managed by

Table 1. Characteristics of enrolled cases in this study

Characteristics	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10	Case 11	Case 12
Age	22	26	30	26	18	23	22	33	26	33	28	29
Body Mass Index(BMI)	Normal	Obese	Obese	Obese	Normal	Normal	Normal	Obese	Obese	Obese	Obese	Normal
Parity	G1P0	G2P1	G2P1	G2P1	G1P0	G1P0	G1P0	G2P1	G2P1	G2P1	G2P1	G2P1
Gestational Age(GA) in week	20	21	16	14	18	12	13	20	11	16	9	13
COVID-19	Mild	Mild	Mild	Asymp.	Mild	Mild	Asymp.	Mild	Mild	Mild	Mild	Mild

Medical treatment, and she was advised to do RT-PCR for COVID-19 infection. The RT-PCR confirmed her as COVID-19 positive without significant symptoms. The patient was discharged. Again RT-PCR for COVID-19 was done after 14 days and found to be negative.

2.5 Case No-5

In this case, an 18 years old woman with normal Body Mass Index (BMI) and Primi Gravida (G1 P0) is admitted to the hospital. She claimed a pregnancy for 18 weeks and per vaginal brownish discharge. The patient did not give any history of fever and other respiratory syndromes and no other medical disorders. She also presented OUT PATIENT DEPARTMENT at her 20-weeks of pregnancy bleeding for one day. The patient having a history of low-grade fever 5 days ago but no other respiratory symptoms. According to the medical examination results the patient was normotensive, afebrile, symphysis fundal height was 16-weeks. Her per vaginal examination found brownish discharge and OS-Closed. However, other initial investigation reports were normal. At the time of her hospital admission, again the US was done and the report was 18 weeks missed-abortion. As there was no remarkable cause of missed-abortion, she was advised to do a test for COVID-19 infection. The RT-PCR test for COVID-19 was positive for the patient. However, the miscarriage was managed successfully and discharged. A follow-up RT-PCR test was again conducted for COVID-19 after 2 weeks of confirmation and it was found to be negative.

2.6 Case No-6

This case was recorded for a 23 years old woman having Primi Gravida (G1 P0). Her Body Mass Index (BMI) I was normal and residing in Dhaka city. Gynecology Emergency unit of the hospital received her with complaints of pregnancy for 13 weeks, feeling feverish. But she had no respiratory syndromes and other medical disorders. On medical investigation, the patient was found normotensive, afebrile, heartbeats 90 /min. However, the US recognized 12-weeks of missed-abortion. Her blood group is A negative (A-ve). All other investigation reports were normal. She was advised to do the test for COVID-19 and the report was positive. The abortion was managed with medical treatment successfully. Again RT-PCR for COVID-19 was done after 2 weeks and found to be Negative.

2.7 Case No-7

The case was for a 22 years old woman with Primi Gravida (G1 P0) living in Dhaka. This case was dealt with in the same hospital with an initial claim for pregnancy for 14 weeks, per vaginal spotting for 2 days, history of contact with COVID-19 patient. However, she did not have a history of respiratory syndromes and other medical complications. Her initial examination report confirmed she was afebrile, normotensive, heartbeats and blood pressure were normal, symphysis fundal height was 12 weeks and per vaginal spotting was present. The US of Pregnancy profile shown 13 weeks missed-abortion. The RT-PCR test for COVID-19 shown a positive result. The abortion was managed with medical treatment successfully and the patient was treated as Symptomatic COVID-19. But per vaginal bleeding was present. After 14 days the US was repeated and found the retained product of conception. It was cleared up by medical treatment. She was advised to do a test for COVID-19 after 21 days and the report was found to be negative.

2.8 Case No-8

An obese 33 years old woman with 2nd Gravida and Para 1 (G2 P1) is admitted to Gynecology Emergency in the hospital with complaints of pregnancy for 24 weeks, absence of fetal movements for the last 20 days known case of hypothyroidism. The patient having a history of hypothyroidism controlled by the drug tablet Thyrox (50 µg) daily and the patient had a history of LSCS. She did not give any history of contact with COVID-19 patients or persons having respiratory symptoms. On examination it was found that the patient is afebrile, normal pulse and BP, symphysis fundal height 20 weeks, fetal heartbeat not audible. The US of pregnancy profile shown 20 weeks of missed-abortion. Other investigation reports were normal. The RT-PCR test for COVID-19 was recommended and found to be positive. Medical treatment was done in the hospital and an RT-PCR was conducted for COVID-19 infection and found to be positive. The patient was discharged and treated as an asymptomatic carrier. Again RT-PCR for COVID-19 was done after 21 days and the report was found negative.

2.9 Case No-9

A 26 years old obese woman with 2nd Gravida and Para 1 (G2 P1) was attended to the

Gynecology Emergency unit with complaints of pregnancy for 15-weeks, per vaginal spotting for 3 days. The patient did not give any history of respiratory symptoms and any other medical and surgical disorders. On Examination the patient was afebrile, normotensive, Symphysis fundal height-12 cm, spotting present. The US of the lower abdomen shown 11-weeks of missed-abortion and other investigation parameters were normal. The RT-PCR for COVID-19 was found to be positive. Abortion was managed successfully and the patient was discharged from the hospital. Again RT-PCR for COVID-19 was repeated after 2 weeks and the report was negative.

2.10 Case No-10

In this case, a 33 years old obese patient with 2nd Gravida and Para 1 (G2 P1) attending in Gynecology Emergency in of the hospital with complaints of pregnancy for 16 weeks, and lower abdominal pain for 1 day. The patient having a history of acute glomerulonephritis (AGN) 2 years ago which was treated conservatively. She had a history of LSCS and she did not have any symptoms associated with COVID-19. On her regular medical examination, the patient was afebrile, normotensive, Symphysis fundal height-14 weeks, per vaginal examination shown OS closed. She was advised to go for an RT-PCR test for COVID-19 found to be positive. Other hematological parameters were normal. The abortion was managed by the hospital. The follow-up RT-PCR test for COVID-19 was repeated 2 weeks later and was found negative.

2.11 Case No-11

A 28 years old obese woman with 2nd Gravida and Para 1 (G2 P1) hailing from Dhaka attending Gynecology Out Patient Department in hospital having claimed for a pregnancy of 11 weeks and a history of fever for 7 days ago. The patient did not give any significant medical or surgical history at this moment but suffering from Diabetes Mellitus which was treated by moderate exercise and Medical Nutritional Therapy. She had no symptoms related to COVID-19 infection. On the examination all the parameters of the patient were normal.

The US of lower abdomen shown 9 weeks missed-abortion. Other hematological parameters were normal. The abortion was managed at the home under the supervision of a gynecologist from the hospital. She was advised to do an RT-PCR test for COVID-19 and found positive. The test was repeated 2 weeks later and was found negative.

2.12 Case No-12

In this case, a 29 years old woman with 2nd Gravida and Para 1 (G2 P1) got admitted to the Labor Ward in the same hospital with complaints of pregnancy for 13 weeks and incidental diagnosis of missed- abortion. The patient having no significant medical and surgical history. She had no symptoms related to COVID-19. The on routine examination the patient was afebrile and the pulse and BP were normal. The RT-PCR for COVID-19 was found to be positive. The abortion was managed successfully. The RT-PCR test for COVID-19 was repeated 2 weeks later and was found negative.

3. DISCUSSION AND CONCLUSION

Coronavirus disease-2019 (COVID-19) has become a global crisis and the vulnerable pregnant group facing risk due to not having a proper guideline for the management of pregnant amid COVID-19. The role of COVID-19 infection is also yet to establish. A few cases of mild COVID-19 pregnant patients had developed perinal demise and mortality [3,11-14]. Here, we are presenting a case series of missed-abortion in pregnant with COVID-19 infection for the first time in Bangladesh. In this case series, we included twelve cases of fetal demise at 11 or more weeks of gestation in women with laboratory-confirmed (RT-PCR) COVID-19 from March 2020 to July 2020 in a single hospital in Dhaka, Bangladesh. The gestational age of the pregnant women was determined from the case history and earlier US scan. The patients did not report any significant causes of abortion therefore, we excluded any other significant clinical and obstetric disorders that may be the cause of abortion other than COVID-19. The COVID-19 infection was confirmed by RT-PCR in the laboratory when they were attending the Gynecology Emergency and OUT PATIENT DEPARTMENT in the hospital. All the patients were managed in this single institute. During the outbreak of COVID-19, the hospital was divided and designated for COVID-19 patient, isolation suite, and non-designated unit. The suspected patients were allowed to get management in isolation suite, and continued to be observed in the isolation ward, and confirmed cases were transferred to the COVID-19 designated area.

Among the twelve cases, most of them were multiparous (11) and only one was nulliparous. Their age distribution was between 18-33 years. Four patients complained of per vaginal bleeding and four patients having a history of mild fever and the rest had no symptoms in association with COVID-19 infection. Regarding co-morbidity one patient had been suffering from Diabetes Mellitus and she was Euglycemic by Medical Nutritional Therapy and moderate exercise. One patient had renal disease and two of them had been suffering from Bronchial Asthma. One patient was Hypothyroid and was Euthyroid by taking the drug. Before management of the patient informed written consent was taken. Abortion was managed clinically according to WHO protocol of missed abortion and COVID-19 was treated as a mild case and there were no life-threatening complications.

In this study, the placental histopathology was not done. However, the SARS COV-2 virus transmission and exact mechanism of abortion was not established yet. There are a couple of hypotheses to explain the intrauterine virus transmission [8]. One is angiotensin-converting enzyme 2 (ACE 2) acts as a surface receptor [15, 16] and another might be the damage of the placental barrier due to maternal hypoxemia [17]. It was also reported in the case study that COVID-19 can induce a placental inflammatory reaction, acute chorioamnionitis, intervilitis, and intense neutrophil [3].

All the cases were managed in multidisciplinary approaches. A limitation of our case series is that we did not collect an autopsy report of the placenta. Another limitation was contract tracing of all patients was not done and we could not conduct the fetal autopsy. However, this case series might be very important to create evidence for future in-depth study for exploring the potential underlying mechanisms. Here, more studies are needed to confirm the clinical causes of the disease and help to make appropriate management protocols in pregnancy during the COVID-19 pandemic.

CONSENT

Before management of the patient informed written consent were taken from all 12 patients.

ETHICAL APPROVAL

This work was approved by the Ethical Committee of Bangabandhu Sheikh Mujib Medical University Hospital.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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