Should Open Surgery or Conservative Management be the Choice for Treatment of Ectopic Pregnancy during COVID-19 Pandemic in a Resource-Poor Setting? A Case Series from India.

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Case Report

Keywords: COVID-19, cesarean scar pregnancy, ectopic pregnancy, SARS-CoV-2 infection

DOI: https://doi.org/10.21203/rs.3.rs-85956/v1

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Abstract

Background: As the COVID-19 pandemic is progressing, it is posing several challenges for management of health emergencies either by direct impact or through the restrictive policies adopted by several nations worldwide. Currently, there is no information on management of ectopic pregnancies associated with COVID-19 in low resource settings. We report the management of three cases of ectopic pregnancies in a limited resource setting and also describe the challenges we faced in managing these cases at a dedicated COVID-19 hospital in India.

Case presentation: T.N. Medical College & B.Y.L. Nair Charitable Hospital (NH) received three asymptomatic, RT-PCR confirmed COVID-19 women with ectopic pregnancy (EP). One was caesarean scar pregnancy (CSP), diagnosed on ultrasound and CT examination and managed with multiple fixed dose methotrexate therapy. Other two cases were ruptured EP managed surgically by laparotomy avoiding laparoscopy to reduce the risk of possible viral transmission.

Conclusions: Based on our experience, we recommend laparotomy as an option for surgical management of EP in resource poor settings. It is useful for prevention of possible transmission of SARS-CoV-2 infection to healthcare workers from surgical smoke and it is wiser to take a conservative approach in managing EP wherever possible. More studies are needed to completely disregard the possibility of presence of viable SARS-CoV-2 particles in surgical smoke. There is a need to formulate specific guidelines to address the collateral damage.

Background

Despite improvements in diagnostic and treatment modalities, ruptured ectopic pregnancy (EP) continues to be an important cause of pregnancy-related mortality and morbidity. CDC has estimated its incidence to be 1-2%[1], yet these pregnancies account for 6% of pregnancy-related deaths[1,2]. It was the leading cause of hemorrhage-related mortality in USA in 2011-2013[3]. Corona virus disease-2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), has emerged as a global health concern since December 2019, spreading to almost more than 200 countries/territories/areas worldwide[4]. Due to its highly contagious nature, many national and regional authorities worldwide enforced the country under lock-down to reduce further spread of the disease. India has undertaken a similar strategy from March 24, 2020 in a phased manner. Hence, non-urgent medical care facilities such as outpatient visits and elective surgical interventions were suspended. Many private and other small-scale hospitals stopped their services to follow enforcement of government issued lockdown orders and some fearing the spread of the disease. This has left pregnant women anxious across the country with the only option of going to state-run hospitals or COVID-19 designated hospitals in the city. Thus, reduced number of accessible medical care facilities and travel restrictions caused patients a significant delay in receiving treatment.
Topiwala National Medical College (TNMC) & B. Y. L. Nair Charitable Hospital (NH) is one such tertiary care public hospital and designated COVID-19 hospital in the city, receiving referrals from across the Mumbai Metropolitan Region[5].

This case report describes the management of three cases of RT-PCR confirmed COVID-19 with ectopic pregnancy including one caesarean scar pregnancy (CSP) (Table 1) and challenges faced in the low resource setting in the initial three months of COVID-19 pandemic (from 4th April, 2020 to 31st July, 2020) in India. The study was approved by Institutional Ethics Committees of ICMR-NIRRH and TNMC, Mumbai.

**Case Presentation**

**Case one**

A 31-year-old gravida 3, para 2 with previous two caesarean sections, presented at around 8-weeks of amenorrhea with three days history of vaginal bleeding. A transvaginal ultrasound scan (TVS) and CT scan confirmed Caesarean scar pregnancy (CSP) with cystic structure of 4x3.2x4cm corresponding to 9-weeks with nonviable fetal pole. A serum beta-human chorionic gonadotrophin (β-HCG) level was 270.27IU/ml. Woman was hemodynamically stable with normal laboratory tests. She was given four doses of Inj. Methotrexate 1mg/kg/day with Inj. Leucovorine 0.1mg/kg/day on alternate days. There was a resolution in the ectopic mass to 4x2.6x2.8cm size after 15 days of first dose. The β-HCG level also dropped to 33.5IU/ml. The patient was subsequently transferred to non-COVID-19 hospital on testing negative for SARS-CoV-2 on RT-PCR for further follow-up which showed a fall in β-HCG to 8IU/ml on day 48 and a complete resolution of a mass on TVS.

**Case Two**

A 27-year-old gravida 2, abortion 1 with 10+5 weeks of amenorrhea presented with two days history of vaginal bleeding and abdominal pain. TVS suggested left sided ruptured EP with moderate hemoperitoneum. β-HCG was 3219.12IU/ml and serum hemoglobin was 8.5g/dl. She was pale but hemodynamically stable. Tenderness in left iliac region on per-abdominal examination and left fornical and cervical motion tenderness on per-vaginal examination confirmed the diagnosis. Emergency laparotomy was done under regional anesthesia which confirmed a 3x3cm ruptured left tubal ectopic pregnancy with around 500ml of hemoperitoneum. Left salpingectomy was performed and the patient was transfused with two units of packed red blood cells. Patient recovered well without needing ICU admission.

**Case Three**

A 30-year-old gravida 3, para 1, abortion 1, presented with intermittent irregular vaginal bleeding since one month and severe abdominal pain since one day. TVS suggested a right tubal EP with 6.1x5.2cm of organized hemorrhage. She was pale with Hemoglobin of 7.6g/dl. Her pulse was 110 beats/min and blood pressure was 130/80 mm of Hg. Right iliac region and cervical motion tenderness confirmed the
diagnosis. Emergency laparotomy was done under regional anesthesia, which confirmed right-sided ruptured ampullary tubal EP organized into a tubo-ovarian mass of around 6x6cm and densely adherent to bowel along with 500ml hemoperitoneum. Right salpingectomy was done after dissecting the mass off bowel and ovary. She received three units of packed red blood cells and recovered well without any complications.

Discussion And Conclusions

To the best of our knowledge, this the first case report from LMICs describing the experience of management of ectopic pregnancies with SARS-CoV-2 infection. In the current COVID-19 pandemic situation with restrictions to routine consultations in outpatient department (OPD) as well as elective operative procedures, there is a delay in receiving treatment for emergency medical ailments like EP. It is needless to say that, all the resources are being used in the attempt of understanding clinical course, management and in prevention of COVID-19. This has inevitably ignored other facets of healthcare such as health conditions which need emergency care. Restrictive measures for limiting the spread of disease and healthcare system disruption during current pandemic is causing patients to lose the crucial time in receiving treatment adding to morbidity and mortality. All three patients received at NH were referred from multiple peripheral or private hospitals.

The prevalence of EP among women presented to an emergency department with first-trimester vaginal bleeding and/or abdominal pain, has been reported to be as high as 18%[6, 7]. Similarly, at NH, the prevalence of EP among women presented with early pregnancy care with abdominal pain and/or vaginal bleeding in pre-pandemic (from 2016-2020) and pandemic period was 18.92% and 17.65% respectively. Recently published analysis from Italy demonstrated increased proportion of ruptured ectopic pregnancies during the lockdown in comparison with the pre-lockdown period[8]. In contrast to this, our hospital data does not show any increase in the incidence of ruptured EP when compared to pre-pandemic period. Since India has been a resource poor country, early pregnancy scan is a rarity, which perhaps delays the diagnosis of un-ruptured EP. This may have contributed to increased incidence (90.91%) of ruptured EP in pre-pandemic period (Table 2). Immediately before the pandemic period (six months) there were 22 women with ruptured EP. However, during the period of pandemic (four months) there were only two cases of ruptured EP, even though NH was the only dedicated COVID-19 Hospital, catering to Mumbai and nearby districts (Table 2).

CSP is one of the rarest sites of EP. Though, the incidence is majorly under reported, it has been estimated to be 1 in 2000 pregnancies[9]. These pregnancies are often associated with severe maternal morbidity and mortality, owing to uterine rupture and hemorrhage. There is insufficient evidence to support either medical or surgical method over each other in managing these cases[10]. Hence, a case-by-case approach is appropriate in deciding the management. We had three cases of CSP in last four years of pre-pandemic period, two were managed medically and one surgically, with no mortality among them. In pre-pandemic period 4.09% of EP were managed by medical method. In current COVID-19 pandemic era, we opted for conservative approach whenever possible in managing EP, avoiding unnecessary surgical
intervention and related risk to both, patient and healthcare workers (HCWs). This also helps in keeping ICU beds vacant for much needy COVID-19 patients. It has been suggested that benefits and risks of different surgical routes should be carefully balanced to select the safest approach for the patient and affirmed that laparotomy can potentially reduce the risk of operating-room exposure to the SARS-CoV-2 virus infection[11]. In an ideal setting, laparoscopy should be the management of choice for EP but in current COVID-19 pandemic situation and in LMICs/resource limited countries, laparotomy is definitely a safer option for prevention of transmission of a virus to healthcare workers (HCWs).

Out of three cases, CSP was successfully managed by fixed multiple doses of Methotrexate therapy and two cases of ruptured EP needed emergency surgical management. Much has been debated and published in a literature regarding safety of open versus laparoscopic surgical procedures in view of transmitting SARS-CoV-2 via surgical smoke plumes. During laparoscopy, there is a theoretical risk of transmitting viral particles in surgical smoke plumes when electrosurgical or ultrasound energy sources are used and because of the pneumoperitoneum, these viral particles could potentially escape into the theater from leakage around a loose trocar seal and during rapid venting through the port site at the time of changing instruments, retrieving specimens, or desufflation at the end of the surgery[12, 13]. Considering this risk, both women underwent laparotomy under regional anesthesia, avoiding potential aerosol generating procedures (AGPs) like general anesthesia, thus maintaining patient’s safety and reducing the risk of disease transmission among HCWs. The experience reported from China and Italy also advocated similar approach[14].

Managing emergency surgeries like ruptured EP in COVID-19 pandemic was challenging as there was no clear guidance from national/international endoscopic societies on safety and use of laparoscopy in COVID-19 patients, also, because of deputation of HCWs across hospitals in managing COVID-19 patients, there is a paucity of experienced HCWs to undertake emergency laparoscopy procedures abiding all the precautionary advices of CO₂ leakage and desufflation techniques which require one to have smoke evacuators or HEPA filters.

The strength of the case series is that all the patients were confirmed cases of SARS-CoV-2 infection on RT-PCR test, they are well characterized, well documented EP cases in early period of pandemic in India. The limitation of the study is the sample size. Larger studies are required to establish our recommendations.

In conclusion, based on our experience, we recommend laparotomy as an option for surgical management of EP as it is useful for prevention of possible transmission of SARS-CoV-2 infection to healthcare workers from surgical smoke and it is wiser to take a conservative approach in managing EP wherever possible. Based on the existing speculations of presence of viable SARS-CoV-2 particles in surgical smoke, further studies are needed to completely disregard this possibility. We also suggest that, in this era of COVID-19 pandemic, there is also a need to address the collateral damage secondary to restrictive policies of authorities affecting other emergency medical or surgical interventions and in terms of delay in seeking treatment.
Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committees of TNMC (No. ECARP/2020/63 dated 27.05.2020) and ICMR-NIRRH (IEC No.D/ICEC/Sci-53/55/2020 dated 04.06.2020).

Consent for publication

Written informed consent was obtained from patients for publication of their Cases. A copy of the written consent is available for review by the Editor of this journal.

Availability of data and materials

All the data reported in the manuscript is presented in the tables. The additional data if needed is available with corresponding authors and can be shared if requested.

Competing interests

The authors declare that they have no conflict of interest.

Funding

No funding was obtained for the study.

Author's contributions

NM and RG had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: RP and NM

Acquisition of data: DT, GK and AP

Analysis, or interpretation of data: All authors

Drafting of the manuscript: RP and NM

Critical revision of the manuscript for important intellectual content: NM, SM and RG.

Statistical analysis: RP and NM

Administrative and technical or material support: NM, SM, RG

All Authors read and approved the manuscript.

Acknowledgements
The authors acknowledge the Director General, ICMR and Network of National Registry of Pregnant women with COVID-19 in India (PregCovid Registry, CTRI/2020/05/025423). The Dean, TNMC, Faculties, Resident doctors in the Department of Obstetrics and Gynecology at TNMC, Mumbai are sincerely acknowledged. RG is an awardee of the DBT Wellcome India alliance clinical and public health intermediate fellowship (Grant no. IA/CPHI/18/1/503933). The manuscript bears No. ICMR-NIRRH/RA/950/07/2020.

**Abbreviations**

**COVID-19**: Corona virus disease 2019

**NH**: B. Y. L. Nair Charitable Hospital, Mumbai, India

**TNMC**: Topiwala National Medical College

**RT-PCR**: Reverse Transcriptase polymerase chain reaction

**EP**: Ectopic Pregnancy

**CSP**: Cesarean Scar Pregnancy

**CDC**: Centers for disease control and prevention

**SARS-CoV-2**: Severe Acute Respiratory Syndrome Corona Virus-2

**MMR**: Mumbai Metropolitan Region

**ICMR-NIRRH**: Indian Council for Medical Research-National Institute for Research in Reproductive Health

**TVS**: Transvaginal Sonography

**βHCG**: β subunit of Human Chorionic Gonadotrophin

**ICU**: Intensive care unit

**OPD**: Outpatient department

**HCWs**: Health Care Workers

**AGP**: Aerosol Generating Procedure

**HEPA**: High efficiency particulate air

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Tables

Table 1: Characteristics of Ectopic Pregnancy Patients with SARS-CoV-2 Infection in India
| Parameters                                      | EP1                  | EP2                  | EP3                  |
|------------------------------------------------|----------------------|----------------------|----------------------|
| Age                                            | 31                   | 27                   | 30                   |
| Socio-economic Status                          | Low                  | Low                  | Low                  |
| Gravida/Parity/Abortion                        | G3P2                 | G2A1                 | G3P1A1               |
| H/O Contact with Positive Person               | No                   | No                   | No                   |
| Indication for COVID-19 RT-PCR testing         | Possible need for surgical intervention | History of possible indirect contact to a confirmed case | Possible need for surgical intervention |
| Weeks of Gestation                             | 9.1                  | 10.5                 | Not Known            |
| Previous Cesarean Section                      | Yes                  | No                   | No                   |
| Spontaneous Conception                         | Yes                  | Yes                  | Yes                  |
| H/O previous episodes of Ectopic Pregnancy     | No                   | No                   | No                   |
| TVS                                            | CSP 40x32x40 mm      | Ruptured Left tubal ectopic pregnancy | Ruptured Right tubal ectopic pregnancy |
| CT Scan                                        | CSP 40x32x40 mm      | Not done             | Not done             |
| TVS and CT scan after 15 days                  | CSP 40x26 x28 mm     |                      |                      |
| TVS after 48 days                              | Complete resolution  |                      |                      |
| βHCG mIU/ml (at the time of admission)         | 270.27               | 3219.12              | Not done             |
| Hb g/dl                                       | 12.8                 | 8.5                  | 7.6                  |
| TLC                                            | 5280/µL              | 10400/µL             | 9600/µL              |
| Blood Group and Rh                             | O+ve                 | O+ve                 | AB +ve               |
| Treatment                                      | Medical method       | -                    | -                    |
|                                                 | Surgical method      | -                    | Yes                  |
|                                                 |                      | Yes                  |                      |
| Blood transfusion                              | No                   | Yes                  | Yes                  |
| Complication                                   | None                 | None                 | None                 |
| Duration of Hospital stay                      | 20                   | 7                    | 7                    |
**RT-PCR**, reverse transcriptase polymerase chain reaction; **ART**, Assisted Reproductive Technology; **IVF**, In-Vitro Fertilization; **TVS**, Transvaginal sonography; **CT**, Computed tomography; **CSP**, caesarean scar pregnancy; **TLC**, total leucocyte count; **βHCG**, beta-human chorionic gonadotrophin

**Table 2:** Comparison of ectopic pregnancy and spontaneous abortion data between pre-pandemic and pandemic period at NH, Mumbai, India

|                        | Pre-pandemic (Jan’16-Mar’20) | Pre-pandemic six months (Oct’19-Mar’20) | Pandemic (April’20-July’20) |
|------------------------|-------------------------------|----------------------------------------|-----------------------------|
| Total EP               | 220                           | 22                                     | 3                           |
| Surgically managed EP  | 211†                          | 22 (all ruptured EP)                   | 2                           |
| Medically managed EP   | 9                             | 0                                      | 1                           |
| Caesarean scar pregnancy | 3‡                          | 0                                      | 1                           |
| Spontaneous Abortions  | 943                           | 157                                    | 14                          |

† 10 un-ruptured tubal EP, 1 CSP and 200 ruptured EP; ‡ 1 managed surgically and 2 managed medically; **MTX**, Methotrexate; **EP**, ectopic pregnancy. **NH Nair Hospital**