

# Premature ovarian failure - A long COVID sequelae

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**ABSTRACT**

Ever since its emergence since 2019, Coronavirus Disease 2019 (COVID-19) has brought the healthcare setup down with its burden of varied appearance and presentation. It can lead to a severe disease with respiratory distress syndrome along with hypercoagulability and various neurological complications. There has been an emergence of a large population of patients who develop a subsequent long term disease known as “long-COVID” which is thought to be secondary to chronic tissue inflammation. We Report a case a 34-year-old female who was infected with COVID-19 12 months back and presented with infertility as a post COVID sequelae. This is the first case report linking Ovarian Failure with COVID-19 in our knowledge.

**Keywords:** Long Covid, Premature ovarian failure, Infertility

**1. INTRODUCTION**

Coronavirus infectious Disease 2019 has emerged as a difficult pandemic with a wide spectrum of presentation and a varied long term sequelae. The Virus is known to affect the Respiratory System as a primary site most often but a enormous count of patients have begun to present with neurological, gastrointestinal, cardiovascular as well as hematological complications as primary symptoms (Wichmann et al., 2020). Not only does the presentation seems to be of broad spectrum but Post COVID sequelae has also been introduced as a very unpredictable complication of COVID-19 (Khalili et al., 2020). Although post COVID complications like myocardial infarction, Stroke and pulmonary embolism have been reported (Jain et al., 2020). Not much stress has been laid over Gynecological complications of COVID-19 which seems to be a neglected domain in this massive pandemic. In the Obstetrics and Gynecology domain COVID has had a great impact not only on the Antenatal and Post Natal Care but also on the domain of Fertility. Ovarian implications of COVID-19 has not been stressed upon and remains a field to be explored, however more concern has been laid over possible pregnancy outcomes, vertical transmission and sexual transmission of COVID-19. Various patients have self-reported changes in their menstrual cycle after they had been affected by the Corona Virus Infectious Disease 2019 (COVID-19). Ovarian Reserve Markers along with Reproductive Hormones seems to be affected due to the ovarian insult by Corona Virus. Effect of COVID-19 disease state and the recovery on the ovaries and its consequences on the menstrual

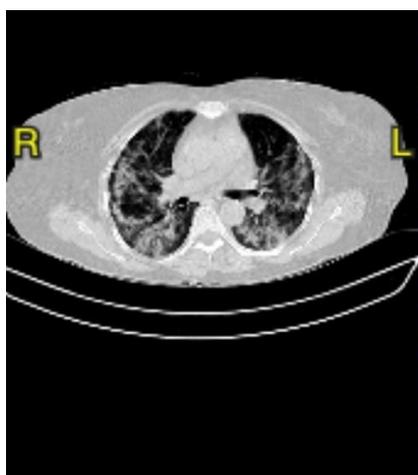


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cycle of the patient, Reproduction potential and endocrine function of the patient are important aspects of COVID-19 infection which is often left undiscussed .We present a case of a 34 year old female who had contracted COVID-19 infection 12 months ago and post recovery had complaint of irregular menses along with infertility.

## 2. CASE REPORT

A 34-year-old female (Gravida 1 Para 1 Live 1) Teacher by occupation, who had COVID-19 infection 12 months ago presented with the complaint of irregular menses and infertility post recovery from COVID-19. She had no history of Fever/Cough/Breathlessness at present. The patient reported to have had admitted for 12 months ago when She had COVID-19 infection of moderate category with a HRCT Chest Ct severity score of 14/25 and CORAD score of 6 (Figure 1). Obstetric History Revealed duration of marriage 7 years, previous pregnancy 5 years back with one live female child conceived normally. Menstrual history revealed Hypomenorrhea with irregularity in menstrual cycle since 12 months. There was No history of use of any contraceptives in the past 12 months. There was no history of previous pelvic diseases or surgery. There was no history of Thyroid Disorder or Tuberculosis in the past. Her Male Partner who was a businessman by occupation had no history of Premature/Retrograde Ejaculation or Any other Sexual dysfunction.



**Figure 1** Showing HRCT of the patient (12 months back) showing ground glass opacity

On General Examination the patient was afebrile, Pulse was 88/min, regular, Blood pressure was 110/70mmhg in right arm supine position and BMI was 20.8 kg/m<sup>2</sup>. On Systemic Examination Bilateral Chest was clear, Normal Heart Sounds were heard, Patient was conscious and oriented and Abdomen was soft, non tender with no organomegaly or mass felt. On Per Speculum Examination Vagina and Cervix was healthy with no evidence of any discharge seen. On per vaginum examination uterus was anteverted, anteflexed with normal size and bilateral fornices free. There was no tenderness present. Patient was admitted for further evaluation. Lab investigations are mentioned in Table 1. Transvaginal Ultrasound was done in which only the stroma was identified in the ovary with very sparse follicles of size less than 1mm (figure 2). Hydrotubation was done which showed no signs of tubal blockage and free fluid in pouch of Douglas post procedure. Patient was planned for Assisted Reproduction Technology and was referred to an ART Centre for the same. Three to Four Day 5 Blastocyst was transferred for implantation in the patient's uterus. Beta HCG levels were monitored and the patient conceived with a positive beta HCG level and urine pregnancy test. Patient's Antenatal Scan revealed a twin pregnancy (Figure 3). Patient was discharged and is doing well on follow up.

**Table 1** showing lab investigations of the case

CBC	Hb-11.3gm/dl MCV-86fl Platelet count-150000/dl WBC Count-8100/dl
LFT	Total Protein-6.6gm/dl, Albumin3.3gm/dl, Globulin3.3gm/dl,

	aspartate aminotransferase 20units/l, alanine aminotransferase 26 units/l, AlkanlinePhophatase 96IU/l, Total Bilirubin :1.0mg/
KFT	Creatinine:0.8mg/dl, Urea 30mg/dl, Sodium 135mmol/l, Potassium -4.3mmol/l
CRP	15 mg/dl
D-Dimer	0.51
AMH	0.34ng/ml
FSH	44 IU/ml
Inhibin B	3 pg/ml
Prolactin	
Estradiol (E2)	25 pg/ml
Thyroid Function Test	Free T3-0.5ng/dl Free T41.1ng/dl TSH-4.9 miU/L



Figure 2 Showing Transvaginal Ultra sound showing features suggestive of Premature Ovarian Failure

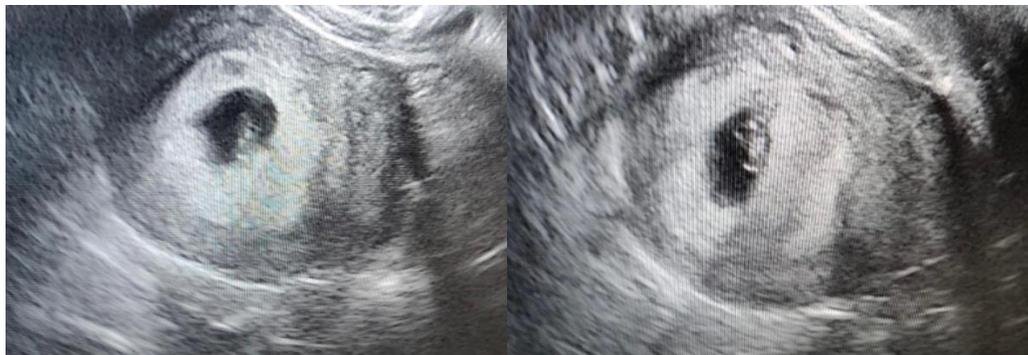


Figure 3 Showing Two Gestational Sacs indicating Twin Pregnancy

### 3. DISCUSSION

Corona Virus Infection 2019 has a broad range of systems as its target beginning from the Respiratory System to Central Nervous System as well as the Cardiovascular System. There have been reports of various complications as a sequelae of COVID-19 which is thought to be due to long term inflammation caused due to Corona Virus known as “Long COVID”. With the increasing complications of COVID-19, its implications on Obstetrics and Gynecology are an emerging field of concern. There have been reports stating increased incidence of COVID-19 in Females with Polycystic Ovarian Disease thus indicating predisposition of COVID-19 in PCOD. However, COVID may lead to infertility and Premature Ovarian Failure in Females who were otherwise having no prior risk factors such as in our case. The Corona virus infects the target cell through binding to angiotensin-converting enzyme 2(ACE 2) and modulating its expression in the cells of the host.

ACE2 is a major component of the Renin Angiotensin System and modulates the amount of Angiotensin II. The postulated mechanism through which the Virus might affect the female reproductive tract thereby causing premature ovarian failure is due to the ACE 2 existence in the Ovary. Angiotensin II and ACE 2 regulate the development of ovarian follicle and ovulation; they also modulate luteal angiogenesis and its degeneration. They also influence the changes in endometrial tissue and embryo development (Kai et al., 2020). Hence SARS COV2 Virus may affect the female reproductive functions through its modulation of ACE2 expression thus causing premature ovarian failure and infertility (Zupin et al., 2020). We have reported a case of 34-year-old female who suffered from COVID-19 12 months back and suffered from irregular menstrual cycle and infertility ever since.

There was absence of any tubal blockage and on Tran’s vaginal ultrasonography only the stroma of the ovary was identified along with few ovarian follicles of less than 1mm. This along with our lab investigations showing low value of AMH lead to a diagnosis of Premature Ovarian Failure and Patient was treated with assisted reproductive technology at an ART Centre and Transfer of the Day 5 Blastocyst which lead to a Twin Conception. It is important to note that other common causes of infertility like thyroid disorder and tubal blockage was ruled out. A recent history of COVID-19 with raised C reactive protein value projects towards a long-term inflammation sequelae of COVID-19.

Also, her partner was evaluated for infertility and was found to be fertile with no sexual dysfunction. All the above findings helped in conclusion of COVID-19 to be the culprit of this premature ovarian failure. This case report highlights the importance of early diagnosis of premature ovarian failure due to COVID-19 and its treatment with a wide range of available assisted reproductive technology.

### 4. CONCLUSION

Thus, we conclude that the physicians along with the obstetricians should be on lookout for infertility in young females who develop p COVID-19 as it may be a rare but a important sequelae of COVID-19 which remains undiscussed and is a uncharted territory. We conclude that more attention needs to paid towards reproductive medicine during the ongoing pandemic. In our case prompt diagnosis of premature ovarian failure along with treatment option of intra cytoplasmic sperm injection and blastocyst transfer lead to a conception of twin pregnancy.

#### **Acknowledgement**

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#### **Conflict of interest**

The Authors have no conflicts of interest that are directly relevant to the content of this clinic-pathological case.

#### **Financial Resources**

There are no financial resources to fund this study.

#### **Informed Consent**

Informed Consent was obtained from the patient.

#### **Author’s contribution**

All the authors contributed equally to the case report.

**Data and materials availability**

All data associated with this study are present in the paper.

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