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The Impact of COVID-19 to Fertility Center in Indonesia: A Brief Report

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Indonesia: A Brief Report

Highlights:
- COVID-19 pandemic affects fertility care in Indonesia
- IVF cycles have been discontinued due to patients testing positive for COVID-19
- COVID-19 has forced fertility centers to modify patient care and staff rotations due to staff shortage
- A clear guideline on IVF and COVID-19 should be laid out in the near future.
**ABSTRACT**

The coronavirus disease 2019 (COVID-19) affected the delivery of care in the fertility center. The higher transmissibility feature of omicron variant increase the transmission possibility between patients, healthcare professionals, and staff. Herein, we report the impact of the COVID-19 pandemic to the fertility center in Indonesia during the third wave period of the pandemic. Seven in vitro fertilization (IVF) cases were cancelled because the patients were tested positive for COVID-19 during their IVF program. Six of the total seventeen medical staff in our center were also tested positive for COVID-19 and stayed at home for self isolation. The cancellation of the IVF program was due to the lack of data regarding safety of IVF procedure in COVID-19 patients, shortage of medical staff, and the lack of negative pressure room in our fertility center. Our priority is to protect the remaining healthy patients in our center as well as the medical staff. The COVID-19 disadvantage both patients, care provider in reproductive healthcare. Regular screening of COVID-19 in fertility setting is highly recommended.

Keywords: COVID-19; IVF; cancellation

**Manuscript**

COVID-19 has severely impacted the access and delivery of medical care, including the assisted reproductive technology (ART) services. The virus has evolved to the current circulating variant, Omicron, with its higher transmissibility compared to previous variants. This significantly increases the risk of infection among patients, healthcare professionals, and staff.

In this case series, we report that seven IVF have had their cycles cancelled due to testing positive for COVID-19 in the latest COVID-19 wave. The cases are reported in line with the SCARE Criteria 2020.(1)

Case 1: A 32-year-old P0A0 presented with primary infertility. She had been married for 8 years. Her husband’s sperm analysis showed an oligoasthenoteratozoospermia and her AMH was 3.08 ng/mL. She was then prescribed with 300 IU of follicle stimulating hormone (FSH) injections for her ovulation. 7 oocytes were retrieved of which 6 oocytes were fertilized (3 were excellent and 3 were good). The next day she tested positive for COVID-19. All embryos were then frozen.

Case 2: A 32-year-old P0A0 with primary infertility have been married for 5 years. Her husband had teratozoospermia and her AMH was 1.43 ng/mL. She was prescribed with 300 IU of FSH injections to stimulate ovulation. 13 oocytes were retrieved. 10 oocytes were fertilized, of which 1 were excellent and 4 were good. Prior to embryo transfer (ET), the patient tested positive for COVID-19. The ET was canceled and all embryos were frozen.

Case 3: A 43-year-old P0A2 with secondary infertility presented to our facility. She had been married for 7 years. Her husband had asthenozoospermia and poor sperm DNA integrity. Her AMH level was 2.81 ng/mL. She was prescribed with 300 IU of FSH injections to stimulate ovulation. She tested positive for COVID-19 during ovulation stimulation, the protocol was stopped, and her cycle was cancelled.

Case 4: A 37-year-old P0A0 with primary infertility presented to our facility. She had been married 6 years. Her AMH level was < 0.01 ng/mL. She was prescribed with 375 IU of FSH and 75 IU of luteinizing hormone (LH) injections to stimulate ovulation. She tested positive for COVID-19 during ovulation stimulation, the protocol was stopped, and her cycle was cancelled.

Case 5: A 37-year-old P1A0, having been married for 12 years, presented to our facility with primary infertility. Her husband had teratozoospermia and hipospermia. Her AMH level was 2.29 ng/mL. She was prescribed with 375 IU of FSH and 75 IU LH injections to stimulate ovulation. She tested positive for COVID-19 before ovum pick up (OPU), the protocol was stopped, and her IVF cycle was cancelled.
Case 6: A 25-year-old P0A3 presented to our facility with secondary infertility. Her husband’s sperm analysis was normal. Her AMH level was 3.28 ng/mL. She was prescribed with 225 IU of FSH and 0.25 mg cetrotide injections to stimulate ovulation. She had 4 frozen embryos, of which 3 were excellent and 1 was good. She tested positive for COVID-19 after Beta hCG. The protocol was stopped and her ET was cancelled.

Case 7: A 30-year-old P0A0 presented with primary infertility to our facility. She had been married for around 4 years. Her husband had asthenozoospermia and her AMH was 3.86 ng/mL. She was then prescribed with 150 IU of FSH injections for her ovulation. 15 oocytes were retrieved. 6 oocytes were fertilized, of which 4 were excellent and 2 were good. The next day, the patient tested positive for COVID-19. All embryos were then frozen.

Currently, Indonesia is suffering from the third wave of COVID-19 pandemic due to the Omicron variant. This has caused a sudden spike in COVID-19 infection among patients, healthcare professionals and administrative staff, including at our facility. This is due to the fertility procedures themselves, as ultrasound and invasive procedures prohibit physical distancing. The Omicron variant also has a higher transmissibility, disallowing proper tracing.

Currently, there is little data on the effect of COVID-19 on fertility, pregnancy, and newborn. Preliminary research suggest no significant impact of COVID-19 to human fertility. There was no differences in ovarian stimulation and embryological variables between the cycles before and after recovering from the COVID-19 infection. Unfortunately, a significantly lower proportion of top-quality embryos was observed.(2) The COVID-19 infection did not affect patients’ performance or ovarian reserve in their immediate subsequent IVF cycle. The authors suggest the IVF treatment might be postponed for at least 3 months after recovering from COVID-19 infection to recruit healthy gametes that were not exposed to COVID-19 infection during their development.(2) The COVID-19 vaccine did not affect the patients' performance or implantation in their subsequent FET cycle and early pregnancy outcome.(3, 4) A retrospective observational study showed there is no difference in the ART outcomes of asymptomatic infertile couples’ before and during COVID-19 pandemic.(5)

However, there are still no available data showing that IVF procedure during COVID-19 was safe and give similar pregnancy outcomes. Furthermore, staff shortages exert an extra burden on the already mounting workload.

So far, our facility has cancelled seven IVF patients due to COVID-19. Four of them tested positive before OPU, requiring them to restart their IVF programs in the future. This leads to additional economic burden, which may affect may affect the patients’ psychological and economical wellbeing. A cross-sectional anonymous survey from a single academic fertility center showed that most participants were distressed by delays in fertility treatments.(6)

The remaining three patients tested positive before ET. Their cycles were cancelled because of the following reasons: the lack of data on the safety and effect of COVID-19 on IVF outcomes; lack of negative pressure theatre at our facility; and eventual staff shortage. At the time of writing, no patient has resumed their cycles post-COVID-19.

At the height of the pandemic, up to 35% (6/17) of our staff were self-isolating at home. Reorganising our team structure and shifts, and regular COVID-19 screening were required. Telemedicine platforms were also adopted to reduce onsite patient visits. We also had to decline admitting new patients, which further disrupted our service, delaying necessary treatments and affecting our financial health. Thus, from our experience, we had to recommend on postponing the cycles until the patients are negative for COVID-19. The cycles may be resumed, at the patients’ discretion, after they recover from COVID-19.
To conclude, the COVID-19 pandemic significantly influences fertility care with patient cancellation and staff shortages a recurring issue. In the future, a specific guideline on when to resume cycles and the specific indications and contraindications to such policy should be decided upon.

Conflicts of Interest
The authors declare that we do not have any conflicts of interests.

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This study does not receive any external funding

Ethical Approval
This study has been exempted from ethical clearance as outlined by the institutional review board.

Consent
Written informed consent was obtained from the patients for publication of this case report

Research Registration
Not applicable as this is a case report

Guarantor
The guarantor of this research is Dian Tjahyadi, M.D. and Kevin Dominique Tjandraprawira, M.D., M.Sc.

Authors Contributions
DT, BR and KDT conceived the study. DT and YMA collected patient data. DT, BR and KDT drafted the manuscript. All authors reviewed the manuscript and approved this final version for publication.

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REFERENCES

1. Agha RA, Franchi T, Sohrabi C, Mathew G, Kerwan A. The SCARE 2020 Guideline: Updating Consensus Surgical Case REport (SCARE) Guidelines. Int J Surg. 2020;84:226-30.
2. Orvieto R, Segev-Zahav A, Aizer A. Does COVID-19 infection influence patients' performance during IVF-ET cycle?: an observational study. Gynecol Endocrinol. 2021;37(10):895-7.
3. Aharon D, Lederman M, Ghofranian A, Hernandez-Nieto C, Canon C, Hanley W, et al. In Vitro Fertilization and Early Pregnancy Outcomes After Coronavirus Disease 2019 (COVID-19) Vaccination. Obstet Gynecol. 2022.
4. Aizer A, Noach-Hirsh M, Dratviman-Storobinsky O, Nahum R, Machtinger R, Yung Y, et al. The effect of coronavirus disease 2019 immunity on frozen-thawed embryo transfer cycles outcome. Fertil Steril. 2022:S0015-282(22)00022-X.
5. Setti PEL, Cirillo F, Immediata V, Morenghi E, Canevissio V, Ronchetti C, et al. First trimester pregnancy outcomes in a large IVF center from the Lombardy County (Italy) during the peak COVID-19 pandemic. Sci Rep. 2021;11(1):16529.
6. Lawson AK, McQueen DB, Swanson AC, Confino R, Feinberg EC, Pavone ME. Psychological distress and postponed fertility care during the COVID-19 pandemic. J Assist Reprod Genet. 2021;38(2):333-41.
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The authors declare that we have no conflicts of interest.

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Ethical Approval
Research studies involving patients require ethical approval. Please state whether approval has been given, name the relevant ethics committee and the state the reference number for their judgement.

The institutional review board determined that our brief report was exempt from an ethical approval.

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Studies on patients or volunteers require ethics committee approval and fully informed written consent which should be documented in the paper.

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N/A as this study does not involve patient participation.

Author contribution

Please specify the contribution of each author to the paper, e.g. study concept or design, data collection, data analysis or interpretation, writing the paper, others, who have contributed in other ways should be listed as contributors.

DT and BR conceived the study. DT, YMA, WP and TD determined the recruitment of patients. DT, BR and KDT wrote the manuscript. KDT, YMA, TD and WP reviewed the manuscript. All authors approved of this version of the manuscript for publication.

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Registrarion of research is not applicable in our case.

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The Guarantor is the one or more people who accept full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish

The guarantors of this study is Dian Tjahyadi as the first author.