

Providing assisted reproduction treatment during the COVID-19 pandemic in Singapore

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The COVID-19 pandemic has posed massive challenges worldwide owing to its high infectivity, presence of asymptomatic carriers and mortality risk, especially in older patients with comorbidities.⁽¹⁾ In severe cases, patients experiencing acute respiratory distress syndrome require prolonged ventilatory support. Singapore's healthcare system moved gradually from Disease Outbreak Response System Condition (DORSCON) Green to DORSCON Orange and then adapted to 'circuit breaker' measures in response to the progress of the pandemic. This called for reorganisation of the national health services to anticipate the increase in COVID-19 cases that might flood the healthcare system. Elective outpatient and non-urgent surgeries were rescheduled to allow for manpower deployment. Here, we describe our experience with provision of fertility care at the largest fertility unit in Singapore at KK Women's and Children's Hospital.

Singapore has experienced an extended period of low fertility rates (total fertility rate of 1.14 in 2018⁽²⁾) despite multiple rounds of governmental, social and financial incentives to encourage procreation. Women are increasingly delaying childbearing till beyond their mid-30s, leading to an inevitable rise in the need for assisted reproduction therapy. Our fertility unit continues to remain fluid in its organisational setup to serve the evolving needs of the population in each distinct phase of the pandemic in Singapore.

DORSCON YELLOW (23 JANUARY–7 FEBRUARY 2020)

In this first phase of COVID-19, high-risk patients were identified by screening their travel history. At-risk patients had to delay any fertility treatment for 14 days after arrival. High-risk patients who had started their treatment cycles were isolated from the general patient pool, and the treatment procedures were performed at the end of the list in full personal protective equipment (PPE). All hard surfaces at these sites were deep cleaned with alcohol wipes between suspected cases.

DORSCON ORANGE (7 FEBRUARY–7 APRIL 2020)

When Singapore's DORSCON level was raised to Orange, new fertility treatment cycles were initially stopped owing to a limited ability to triage patients. There were also concerns regarding the effects of COVID-19 on pregnancy outcomes.^(3,4) Patients

undergoing ovarian stimulation were advised regarding the possibility of cycle segmentation with freezing of all embryos for transfer at a later date. Symptomatic patients were isolated to cancel the cycle to limit spread of the disease. This was done alongside other mitigation measures implemented hospital-wide, including twice-daily temperature monitoring for staff, physical distancing measures, teleconferencing in place of physical meetings, obligatory surgical masks in clinical areas and mandatory five-day medical leave for anyone with acute respiratory symptoms.

From 12 February 2020, in-house testing for COVID-19 with a minimum four-hour turnaround time became available. This was done via a nasopharyngeal swab that detected the coronavirus, SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), via real-time reverse transcription-polymerase chain reaction. The availability of this swab allowed proper triage of at-risk patients and supported our decision to resume assisted reproductive cycles. At-risk patients included patients with symptoms of acute respiratory disease and those with a travel or contact history with confirmed cases. Nevertheless, all patients were advised to delay their fertility treatments, given the evolving COVID-19 situation in Singapore. In most cases, postponing assisted reproductive cycles by a few months is unlikely to significantly impact the chances of success. These measures resulted in a 30% reduction in treatment cycles compared with the same time period in the previous year.

Patients initiating new treatment cycles were first screened for general well-being via telephony, and comprehensive screening was completed on arrival. Patients with acute respiratory symptoms, travel or contact history were requested to postpone their appointments. Only one accompanying person was allowed, who was also subjected to the same screening measures. Patients received written information regarding possible cycle cancellation should there be a rise in the DORSCON level or if they were at risk of COVID-19 infection. Other measures to reduce the risk of viral transmission included: (a) staggered clinic visits for follicular tracking reviews to minimise crowding in the waiting room, (b) physical distance of at least 1 m between seats and (c) optimised workflow to minimise the time that each patient spent in the hospital. Allocated time slots were based on the last digit of the patient's identity card numbers. Our patient waiting area can hold up to 25 patients with social distancing measures in place. In-cycle patients with acute respiratory symptoms and possible contact history who met the Singapore Ministry of Health's case

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definition of COVID-19 were isolated until their COVID-19 swab collection was completed. They were informed of their results over the phone.

Oocyte pick-up (OPU) and embryo transfer procedures were conducted in different rooms. OPU was conducted under intravenous propofol sedation, with the anaesthetic team in full PPE (i.e. N95, goggles and waterproof suits). Additional time was provided between cases for wearing proper PPE gowns and for deep cleaning with alcohol wipes. High-risk cases with acute respiratory symptoms or relevant contact history were scheduled at the end of the list in a negative pressure operating room. They were first assessed for fitness for OPU. A portable gassed incubator was used to transport the follicle aspirates safely from the negative pressure operating room to the *in vitro* fertilisation laboratory to minimise impact on oocyte quality.

Embryology laboratory considerations in the face of COVID-19 included the usual requirement of surgical masks at all times and appropriate PPE for isolation cases. Physical distancing measures and working in split teams were enforced, and high-touch surfaces were wiped down with alcohol, with adequate airing in between to minimise aerosol build-up.

CIRCUIT BREAKER (FROM 7 APRIL 2020)

In the third phase of the COVID-19 epidemic, all non-essential services in Singapore were stopped. This circuit breaker is Singapore's version of a limited lockdown or movement control order. Assisted reproduction services were classified as being essential. However, in view of the heightened risk of local transmission, only time-sensitive assisted reproduction cycles were being initiated. Patients included older women and women with poor prognosis, such as those with low ovarian reserves or previous poor ovarian response, or other time-sensitive situations such as medically indicated fertility preservation for oncological conditions. All other cases are advised to delay their treatment. From 24 April 2020, no new cycles were being started unless they met the time-sensitive criteria.

PROVIDING FERTILITY TREATMENT DURING DORCON ORANGE AND CIRCUIT BREAKER

Should we offer assisted reproductive therapies in the midst of the COVID-19 pandemic? Several reproductive medicine societies have issued recommendations regarding elective fertility treatments. The largest among them, the European Society of Human Reproduction and Embryology, recommended a precautionary approach for all patients considering fertility treatment and advised against pregnancy at this time. For patients already undergoing treatment, it has suggested deferring pregnancy with oocyte or embryo freezing.⁽⁵⁾ The American Society for Reproductive Medicine (ASRM) has also recommended against initiation of new treatment cycles and

to cancel all embryo transfers.⁽⁶⁾ However, the ASRM clarified that infertility is a disease and that infertility treatment is not regarded as elective.⁽⁷⁾ With the deteriorating situation in the United Kingdom, the Human Fertilisation and Embryology Authority ordered all procedures to be stopped on 15 April 2020.⁽⁸⁾

At the time of writing, no patients with COVID-19 are undergoing assisted reproductive treatment in our centre. The reduction of cases is in line with our national circuit breaker restrictions. As the circuit breaker is ongoing, further reductions in community cases are expected. Resumption of the full service at the end of the circuit breaker should be approached cautiously so as to prevent a second wave of coronavirus infection.

Infertility is a well-defined disease that afflicts approximately one in seven couples.⁽⁹⁾ A woman's reproductive reserve is finite, and the timing of reproductive treatment directly influences the probability of reproductive success. While the number of COVID-19 cases in Singapore is presently increasing, the strict nationwide measures, enhanced screening and reduction of footfall at the hospital during the circuit breaker period allowed us to continue to offer assisted reproductive therapies to patients with time-sensitive indications while keeping cross-infection to a minimum. To date, there has been limited evidence of increased severity of COVID-19 in pregnancy or vertical transmission of COVID-19 to the baby.^(3,4) By providing timely and safe fertility treatment, we strive to give couples something to cheer about amid this pandemic.

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