ART services and COVID – 19–SARs 2–lessons to be learnt

EDITOR IN CHIEF

COVID-19–SARs2 pandemic has changed the way the world used to be before December 2019. On this day, when I am writing this editorial, more than 64 million total cases with 18.5 million active cases have been reported globally. More than 1.5 million deaths and still oscillating positive counts is a sign that the situation is not going to change soon. The situation in India is not different (9.5 million total cases/4 lakh active/1.38 lakh dead/31 thousand daily cases). The only hope is to stop or at least put a break on the morbidity and mortality caused by this deadly infection is by innovation of vaccine. By the time this article is published, vaccination seems to be a reality now at least for frontline health workers.

Because of restrictions of lockdown, uncertainty and lack of information on the effect of SARs2 on reproduction, sperm, egg, and embryo, most countries cancelled all assisted reproductive technology (ART) programs, and even all fertility treatments in the beginning. But with the passage of time more information and literature poured in and various societies like The American Society for Reproductive Medicine (ASRM), European Society of human reproduction (ESHRE), and The International Federation of Fertility Societies (IFFS), Indian Fertility Society (IFS) and Indian Society of Assisted Reproduction (ISAR) issued the recommendations to open up the ART services though with lot of restrictions. In India, Indian Fertility Society, Indian Society for Assisted Reproduction, and ACE jointly formed a task force and issued a joint statement suggesting do's and don'ts to its members. Initially the services were opened for select group of patients like poor responders, frozen embryo transfers, and for patients requiring fertility preservation. However, fresh cycles and third party reproduction remained restricted for quite some time initially because of lack of clarity but these also opened slowly later on. These recommendations came at a time when the pandemic was still at its peak in many countries including India, and more and more cases were being added. This was also the time when scientists and researchers were working overtime to collect relevant information of the effect of Sars2 virus on sperm, egg, embryos, and reproduction as whole. This time also saw an unprecedented uncertainty among the practitioners as well as infertile couples whose treatment was interrupted for an indefinite period. In spite of recommendations issued by various societies, there were lots of doubt in the minds of both clinicians and patients regarding the ill effects of SAR2 on the pregnancy, risk of transmission during ART procedures like IVF and ICSI, during pregnancy, risk of miscarriage and risk of transmission during delivery.

If we look back at the research conducted during this pandemic on Sars2 and human reproduction, there has been a remarkable progress on that front. Till September there were only 78 relevant papers published on the subject, which have increased to 124 by the first week of December and lot of information has been added over a period, which has helped in clarifying lot of dilemmas and grey areas. However, still more information and data needs to be collected, analyzed, and used for clinical application.

Viral infection-related gene expression studies and RNA sequencing data studies have identified that the presence of ACE 2 and protease transmembrane protease serine 2 (TMPRSS2) expression is a must for corona virus infection to affect any cell or tissue. They are known as entry factors. Using this knowledge, various authors have studied the coexpression of ACE2 and TMPRSS2 in various reproductive tissue, both in male and female namely sperms, oocytes, cleavage stage embryos, blastocyst, and endometrium. Based on these studies, we now know that coexpression is very rare and is seen only on spermatogonia and not seen on sperms, so there is no evidence to suggest that covid virus is present in ejaculate and there is no data to suggest the avoidance of intercourse. Seminal parameters are affected because of generalized effect of viral infection. Oocyte and ovary appear to be protected from covid virus infection because of lack of entry factor on them. On the other hand, human embryo seems to have expression of both ACE2 and TMPRSS2 after day 6 (postimplantation stage) while early embryo are spared and are not susceptible to infection as there is no expression of these entry factors however more studies are required to confirm this finding. Susceptibility of endometrium was also studied and it was found to have low expression of ACE2 and medium expression

of TMPRSS2. More inputs and research on the long-term follow up and effect on both male and female reproduction is required and it is the duty of all involved to pool in the data in coming future so that the answers to major reproductive dilemmas post SARs infection becomes available.

There is also a need to make patient friendly education programs, to create awareness among infertile couples. International Societies like ESHRE, ASRM, and IFFS and national societies like IFS, ISAR, and The Federation of Obstetric and Gynaecological Societies of India (FOGSI) are already working toward collecting the data from various sources, monitoring the trends, organizing surveys, and studying the effect of covid infection on pregnancies and newborn. There is a need to have a collaborative effort at all levels to pool in the data and come out with clear cut massage for all clinicians involved in reproductive medicine globally.

Till than all reproductive medicine professionals should continue to take all precautions to minimize the risk of viral transmission, avoid unnecessary interventions, do the proper risk assessment, devise clear safety plans for patients and staff, document all active case, there effect on pregnancy and long-term effects on reproductive health and newborn health. The lessons learnt from this pandemic will go a long way in improving the understanding and managing such crisis in the future.[1-4]

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