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Viewpoint Article

IVF laboratory management in COVID-19 pandemic

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Abstract

Background: Since the first report of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), widely known as COVID-19, in late December 2019, it has spread worldwide. The eventual return of new normal has started to happen in most countries where the COVID-19 curve has flattened, and Assisted reproduction technology (ART) services are eventually resuming. Well-organized ART (embryology/andrology) laboratories safeguard the wellbeing of all staff, patients, and their gametes/embryos.

Main body: A well-organized pandemic management plan must be implemented in anticipation of possible subsequent COVID-19 waves. Apart from local and national guidelines, some mandatory changes need to be taken into considerations that will allow us to overcome the fear of this deadly pandemic, work smoothly and stop any possible transmission without comprising the quality control for successful treatment. These mandatory changes include conserving different supplies, reducing manpower needs, and various protective measures for non-clinical and clinical staff, patients, and gametes/embryos.

Conclusion: The current pandemic of COVID-19 suggests a well-organized action-oriented emergency plan to assure the wellbeing of all stakeholders.

Keywords: COVID-19, Infertility, Response plan, IVF Laboratory, embryology, and Andrology Laboratories, India

Background

Within the last two decades, severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS) emerged as highly pathogenic and were responsible for major respiratory disease outbreaks. The recent deadly human Coronavirus (SARS-CoV-2) in cells is mediated by using angiotensin-converting enzyme 2 (ACE2) receptors by binding with a 1273 amino acid, long spike (S) viral protein protruding a 'corona' like appearance [1]. ACE2 receptors have been reported in Leydig, Sertoli, theca, granulosa cells of the human ovary, and spermatogonia of the human testis [2]. Globally, the health care system has been under an unprecedented strain introduced by the COVID-19 pandemic, and to stop the spreading of SARS-CoV-2, all non-essential care treatments were discontinued in numerous countries. Although assisted reproductive technology (ART) also comes under the "non-essential" healthcare system, various international groups, and bodies such as the American Society for Reproductive Medicine (ASRM), European Society of Human Reproduction and Embryology (ESHRE), and British Fertility Society (BFS), raised the concern regarding discontinuing fertility treatments resulting in generating a difference of opinion to what to be considered as essential or non-essential. After the world health organization (WHO) announced COVID-19 as a pandemic, fertility treatments were suspended, as recommended by various fertility societies, including ASRM, ESHRE BFS, raising anxieties in patients with fertility issues [3]. Although, from June 2020 onwards, there has been some resumption in the ART treatment, however, there are still discrepancies regarding the manner and the extent of ART treatment to be offered. Although the COVID-19 pandemic has affected both public and private centers, all fertility societies have gradually recommended the resumption of ART treatment, highlighting the early identification of patients requiring immediate treatment [4].

Positive Hope

The viral presence in the reproductive tract in males affects fertility and highly increases the risks of sexually transmitted infections [5]. Up to date, the extent of existence and replication of viruses in the male reproductive system is not clear [6]; however, the Zika virus has been reported to stay up to one year in males after recovering from infection [7]. Salam and Horby [8] reported the transmission of 27 viruses in male semen [8]. Moreover, structural stability plays a vital role in this shedding

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process. Li D et al. [9] reported the transmission of COVID-19 into semen [9]; however, biases like low sample size, the stage of infection, and the time of the study (COVID-19 pandemic) altered the result. Furthermore, there was no cross-contamination of cryopreserved semen samples has been reported yet.

Mandatory changes

Per the centers for disease control and prevention (CDC) safety standards, it was mandatory for all front-line staff to use personal protective equipment (PPE), including face masks, disposable laboratory coats, eye protectors, and shoe covers. At least two alternate mini-teams should be made available to limit the spread of the virus if any staff is infected. In case of any staff being infected, at least two alternate mini-teams should be available to limit the spread of the virus. Proper safety measures should be followed, and all staff should be appropriately educated. Proper face masks and distance should be maintained and contact with patients should be avoided. Non-laboratory (clinicians and nurses) and non-medical (security, technicians) persons should be trained for liquid nitrogen tank filling under video conference call with embryologists for cryopreserved samples if lab staff is quarantined. Proper sanitization of equipment, devices, and workspace with detergents, UV irradiation, and disinfectants with proven efficiency should be performed after every procedure. In times of peak spread, the use of telehealth technologies in video conferencing and phone consultation should be given preference over the in-person face-to-face interactions. Honest counseling about the cycle cancellation in case of COVID-19 positive test before the stimulation, in-between stimulation, and before trigger should be done in advance. Apart from this, as the effect of COVID-19 infection on sperm, oocytes, embryos, implantation, and miscarriages is still unknown, it should also be discussed with the patient.

All the persons (both staff and patients) entering any fertility clinic should fill the ART Triage questionnaire to understand any potential source of infection [10]. Any potential infectious case should be referred to COVID-19 testing according to local and national guidelines. Some Basic recommendations as an early-level response plan in pre-pandemic management for ART laboratories are listed below in Table 1.

Andrology Laboratory Recommendations

As some studies have reported the possible viral transmission in either semen or testicular sample, proper necessary measures should be taken. Some possible recommendations needed to be made summarized in Table 2.

Embryology Laboratory Recommendations

For smooth working of embryology laboratories in COVID-19 pandemic, certain recommended precautions that need to be taken are summarized in Table 3.

Non-laboratory Recommendations

All the possible transmission ways should be blocked starting from by proper 6-step hand-washing at entry before entering the laboratory, use of PPE kits by all staff, well-organized mini-teams of staff, cutting down in-person interactions within laboratory staff and with patients, a proper social distancing between patients and staff, introduction of alarm sensors system in liquid nitrogen tanks, proper backup of all essential commodities, and removing outer packing of all media. Moreover, consumables should be adequately monitored and removed before taking inside the laboratory, avoiding unnecessary movement, extra mobile air filters, shearing of pens and papers should be discouraged, and door handle should be cleaned frequently.

Table 1: Early-level recommendations for ART laboratories to stop COVID-19 transmission.

Recommendation	Basis of evidence
A spare cryogenic storage tank should be available to store sufficient liquid nitrogen in case of possible Lockdown.	Practice Committees of the American Society for Reproductive Medicine, Society for Reproductive Biologists and Technologists, and Society for Assisted Reproductive Technology [11].
Maintaining records online.	Practice Committee of Society for Assisted Reproductive Technology; Practice Committee of American Society for Reproductive Medicine [12].
Wearing proper masks and PPE kits to stop cross-contamination.	Recommendation based on expert opinion.
Vaccinating all staff on a priority basis.	World Health Organization [13].
Preparing emergency contact list for all clinical and non-clinical staff.	ESHRE Guideline Group on Good Practice in IVF Labs et al., 2016 [14].
Educating the possible disease transmission and mitigation methods to all staff.	Kuhar et al., 2019 [15].

Summary and Conclusion

COVID-19 pandemic has a severe risk for all healthcare workers and patients, including IVF laboratory workers. Any accidental exposure of contaminated fluids or materials poses a direct concern for IVF healthcare workers. Most of the standard operating procedures (SOP) are inadequate to face the aerosol-mediated transmission of viruses. All SOPs should be revised following the national and local guidelines, with strict implementations to withstand future infections. Good collaboration between different units and team members is mandatory for smooth functioning when running IVF laboratories in times of crisis, such as the current COVID-19 pandemic.

Table 2: Andrology laboratory recommendations during COVID-19

Recommendation	Basis of evidence
As a precautionary measure, all males starting their fertility treatments should be tested for COVID-19.	Practice Committee of Society for Assisted Reproductive Technology; Practice Committee of American Society for Reproductive Medicine [12].
Fertility preservation should be considered invulnerable males, including males undergoing therapy and autoimmune and inflammatory treatments.	Esteves et al [16].
Where planned, a proper dedicated area of semen collection and separate semen cryopreservation tank should be assigned.	Andrabi et al [17].
A proper semen collection written instruction in local and national language should always be available in the collection room before sample collection to avoid in-person contact.	Andrabi et al [17].
All andrology technicians/embryologists should strictly follow the standard operating protocols in handling the semen samples.	Onigbinde et al [18].
Proper filtration systems should be installed in the form of mobile towers to increase air quality inside the andrology laboratory.	Recommendation based on expert opinion
All the materials used in performing andrological procedures should be disposed of immediately after the procedure, followed by thorough cleaning.	Recommendation based on expert opinion
In COVID-19 positive patients, home collection and proper care can be an ideal way.	Recommendation based on expert opinion

Table 3: Embryology laboratory recommendations during COVID-19

Recommendation	Basis of evidence
Avoiding in-person counseling and use of tele phone or email calling. Adequate time should be given between procedures when performing a thorough cleaning in ovum pickup areas.	Andrabi et al [17].
Minimal embryology teams should be made available for worst-case scenarios.	Andrabi et al [17].
Extra care should be taken in follicular fluid handling during screening procedures, especially in COVID-19 infection recovered patients.	Recommendation based on expert opinion
After the proper follicular fluid screening, care should be taken in the form of non-spillage of fluid, proper closing of the lid, and immediate disposal should be taken care of.	Recommendation based on expert opinion
Pipette holders should be disinfected after every oocyte retrieval procedure.	Recommendation based on expert opinion
Although no cross-contamination of gametes or embryos has been reported yet; however, it is better to use a closed type vitrification system that avoids direct contact of embryos with liquid nitrogen.	Porcu et al [19]
A separate liquid nitrogen tank should store cryopreserved embryos and oocytes of patients having symptoms or tested positive for COVID-19.	Recommendation based on expert opinion
After every procedure, proper disinfection of the workstation and other equipment should be done with disinfectant, which is alcohol-free, non-VOC releasing, non-fragranced, and effective against bacteria, yeasts, viruses, and mycobactericidal.	Alaluf et al [20]
Although the chances of cross-contamination are very low in ART laboratories due to antibiotics in media and continuous washing of gametes repeatedly, every laboratory should properly follow its standard operating protocols.	Onigbinde et al [18]
Some other suggestions during this COVID-19 pandemic period include, following routine good laboratory practice, proper protection of staff, proper cleaning of safety cabinets with tested quaternary ammonium compounds lab disinfectants, proper pre and post sanitization of all equipment, bed, trolley, and theatre (General suggestions).	Recommendation based on expert opinion

Abbreviation

COVID-19: Coronavirus Disease 19; WHO: World Health Organization; ART: Assisted Reproductive Techniques; IVF: In-Vitro Fertilization; SARS-CoV-2: Severe Acute Respiratory Coronavirus 2; ASRM: American Society for Reproductive Medicine; ESHRE: European Society of Human Reproduction and Embryology; BFS: British Fertility Society; ACE2: Angiotensin-Converting Enzyme 2; CDC: Centers for Disease Control and Prevention; PPE: Personal Protective Equipment

Declaration

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Availability of data and materials

Data will be available by emailing wasiandrabi@gmail.com.

Authors' contributions

Syed Waseem Andrabi (SWA) and Puneet Rana Arora (PRA) are the principal investigators of this manuscript (Viewpoint). SWA is the responsible author for the study concept, design, and writing. PRA is responsible for reviewing and editing the manuscript in its final form. Jaffar Mir (MJ) approved the final manuscript.

Ethics approval and consent to participate

We conducted the research following the Declaration of Helsinki. However, "Viewpoint Article" need no ethics committee approval.

Consent for publication

Not applicable

Competing interest

The authors declare that they have no competing interests.

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