

Influence of COVID-19 Pandemic on Assisted Reproductive Techniques Services in India: A Review

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ABSTRACT

The COVID-19 pandemic and strict restrictions during the lockdown in India have adversely affected reproductive services such as assisted reproductive techniques, abortion, and family planning techniques. Many problems are faced during this pandemic era by both patients and medical representatives. Globally 0.3% of all infants born every year are conceived using assisted reproductive techniques. But during the COVID-19 pandemic, professional organizations recommended a moratorium on infertility services which made couples suffer a lot. Around 90% drop was observed in several people undergoing *in vitro* fertilization (IVF) cycles and significant reductions were observed in patients undergoing fertility treatment in the country. COVID-19 also challenges all medical specialities, trying to provide safe and essential care for fertility treatments. Clinical development has evolved tremendously through safe, new technologies and ways of optimization and planning for clinical trials of infertility treatments. In future, we need to develop clear and modified plans to ensure the ability to provide care while maximizing the safety of current regarding new medical findings. These recommendations provide resources for restarting Assisted Reproductive Technology (ART) practices again.

Key-words: Assisted reproductive technology (ART), COVID-19, Fertility centres, Infertility, Telemedicine

INTRODUCTION

The world is facing a novel coronavirus disease (COVID-19) that has spread quickly because of its rapid community transmission, high virulence, and sustained surface viability. This pandemic presents a unique global challenge on a scale not previously seen, the infectivity and mortality rates higher than previous pandemics, and diseases are present in almost every country. It caused approximately 140 million confirmed cases, with about 3 million deaths worldwide until April 18, 2021 [1]. COVID-19 adversely affected the people, professions, and world economy at an enormous level. The effect on people's health, physical and psychological has been unexplainable.

Recently governments around the world announced the most far-reaching restrictions of personal freedom in modern history due to COVID-19. The rapidly increased COVID-19 cases raise the prospect of massive hospitalization on the health care system in the world can manage [2]. The world is in a medically daunting position. Several professional organizations urgently cancelled all infertility services including medically assisted reproduction and ART technology inventions and all fertility treatments except for fertility preservation in patients exposed to gonad toxic chemotherapy and radiotherapy. Several fertility societies [3-11] worldwide responded by recommending that fertility clinics cease IVF treatment, except essential medical fertility preservation, to protect staff and patients from unnecessary exposure to the virus (particularly given the unknown risk during pregnancy), while also allowing resources to be redeployed to frontline medical staff treating COVID-19 patients. The decision to close, or sharply reduce, the clinical operation of IVF clinics, led to a shift in the management

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of IVF laboratories in three phases: shutdown preparation; shutdown maintenance; and restart. Reasons listed for understanding these extraordinary measures prevention of possible complications of ART and medically assisted reproduction and virus-induced complications of pregnancy including the potential vertical transmission of the fetus and optimization of critical new death care resources. The COVID-19 pandemic gave rise to an immediate dilemma for centres, which are treating infertile couples with medically assisted reproduction and ART. Apart from the deaths and after-effects of the virus, couples are facing

other grave situation-becoming parents. Because of the second lockdown, which was applied due to the second wave of COVID a delay can cause further emotional disturbance for many such women who were trying to have children. The burden, thus, remains for the fertility treatments providers to put their patients' minds at ease and help them as best as they can [12]. For the control of stress during the outbreak of this pandemic, several ways to manage such type of psychological intervention are by using therapeutic dialogues, inducing hope, listening and support and face to face counseling which should be offered by the healthcare workers (Fig. 1).

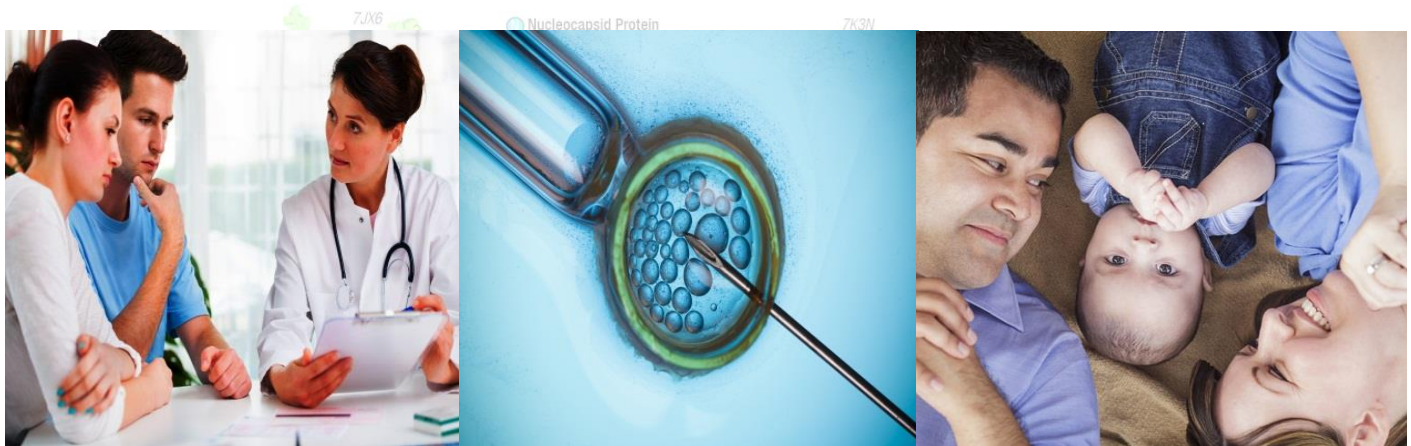


Fig. 1: Infertility counseling, assisted reproductive technology and family planning (Source electronic media)

In recent times, fertility issues have risen amongst couples of all ages and they are choosing medical help to become parents. Consequently, *in vitro* fertilization (IVF) has become a popular option to becoming a parent; however the covid-19 situation has complicated the very extensive treatment.

Since March 2020, Covid 19 pandemic has traumatized the whole world with its transmission across all the countries, without making any differences whether poor or rich, have well-established health care facilities or not. Lockdown is the only measure to check the effects, impact of adverse mental, physiological, stress, anxiety, psychosocial, nervous disorder and economic consequences. Still; there is no safe, effective preventive treatment without causing a side effect in users. During the COVID-19 outbreak, imposed lockdowns and compulsory quarantines increased levels of tension [14]. However vaccines developed and introduced, but it is not 100 per cent effective. Social distancing, respiratory hygiene remain the two most effective preventive strategies for precautions [15,16]. Use of networking online

platforms to work from home, in teaching, tele-consultation, healthcare and management increased use of radiations during the pandemic also creates stress affects physiology and caused social-economic imbalances [17,18]. Besides physiological and psychological effects of Covid-19, very drastic changes/effects have been observed in infertility clinical and counseling issues services, reproductive health care services and Assisted Reproductive Technology services [19]. Therefore, the main aim of this review is to summarize current knowledge regarding the effect of covid-19 on patients and medical specialities and also suggest reproduction techniques, medical specialities to help to solve this problem.

Effect on patients and suggestions- The unprecedented covid-19 calamity has emerged as a great challenge for the whole world, the doctors and the medical fraternity along with couples seeking infertility treatments in India. Medical experts pointed out that 30 lakh people seek fertility treatment in India every year but only 5 lakh of them undergo IVF procedures but during the covid-19

pandemic, couples have suffered a lot, as per data analysis, from April to June 2021 almost 90% drop was observed in the number of people undergoing IVF cycles across India. The volume of IVF cycles performed annually has seen a dip during the pandemic. In India, about 250,000 IVF cycles are performed in a year, which we estimate to have gone down to 150,000-180,000 in 2020. This is disturbing news because IVF treatment not only helps women to conceive safely but also identify any other underlying ailment they may be suffering from [20]. Experts said most of the couples had to postpone their plans of parenthood and some had to leave their treatment uncompleted. There was a significant reduction in patients undergoing fertility treatment in the country. As every moment matters in this procedure to begin parenthood through IVF, are going through an emotional roller coaster.

IVF is the most effective and common treatment of infertility. Patients face several problems, where each step begins on a proper timeline scheduled and leads to the next consecutive step. With the lockdown in the apprehension of covid-19, the treatment and ongoing steps in the timeline of the couple's undergoing treatment had to make an unexpected stop. This led to a disturbance in the schedule of the treatment of huge emotional dissatisfaction and uncertainly comes among couples, who badly wanted a baby [21,22]. Besides this one more problem was occurred that was a travelling problem that played a part in the failure of IVF treatments.

With international boards closed and travel coming to a standstill IVF related medical tourism would certainly get impacted. This current situation will impact all Asian countries which have been attracting international patients. These international patients have either cancelled or postponed their infertility treatments due to travel restrictions as well as fear of the covid-19 pandemic [23]. Their all problems led to financial loss and mental depression among patients.

This is a very challenging time for patients with fertility. Many optional changes are being considered. In March, when covid-19 Pandemic hit Massachusetts, centres providing infertility services were forced to hit the pause button, leaving many couples in the United States hanging. On March 17, the American Society of reproduction (ASRM) issued guidelines for fertility specialities, which provided five key recommendations, including the suspension of new treatment cycles and the cancellation of embryo transfer, as well as delayed elective surgeries exception in only those cases, where the patients are currently in the cycle or who require urgent fertility preservation due to cancer treatment [24,25]. Their recommendations were made with a sanguine view of the Pandemics trajectory. Most recent guidelines support the gradual and judicious resumption of the delivery of reproductive care. A recent article suggests some changes in the delivery of testing kits and the interconnected digital technologies such as telemedicine appointments, syndromic surveillance, visualization tools and connect- tracing apps etc (Fig. 2).

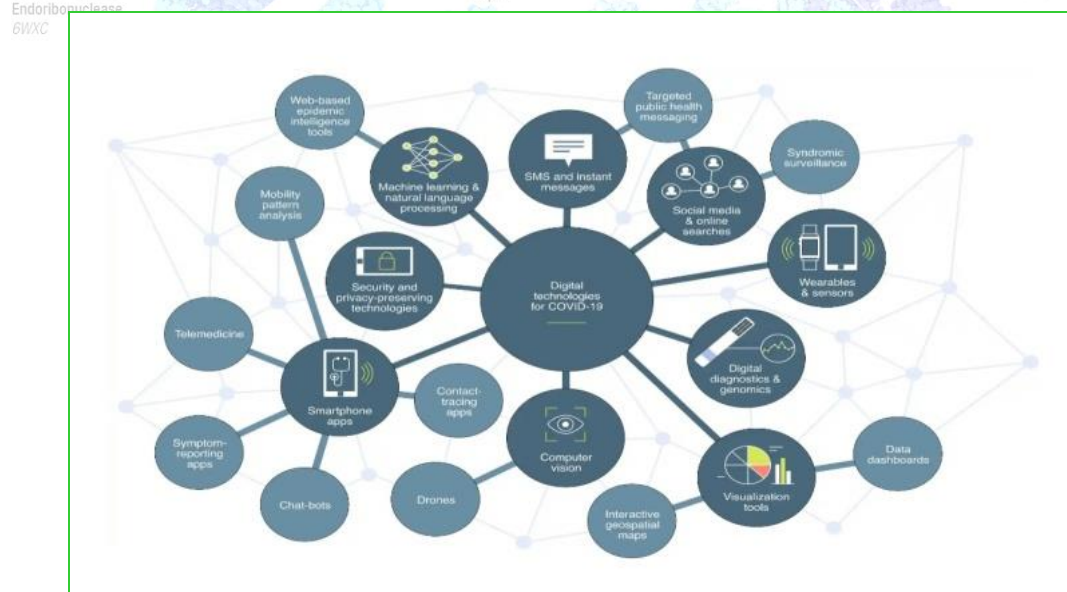


Fig. 2: The interconnected digital technologies used in the public health response to COVID-19. (Source: Digital technologies in the public-health response to COVID) [25]

We all know that we are not aware of when the pandemic is going to be completely over. It is very difficult to say whether it will be 6 more months, 1 year, 2 years, 5 years, or forever. The pandemic will stay until we either develop strong immunity or a vaccine gets discovered and we know that infertility treatment time is sensitive and stressful. Under the best circumstances, infertility is a time full of uncertainty and emotional challenges. The conditions created by the covid-19 pandemic certainly add to that stress.

Some things help reduce stress. The clinic can provide a referral to a trained mental health provider who can consult with the patient, how to manage stress and emotions surrounding this extremely difficult set of

circumstances. Doctors suggest that it is better to hold the procedure temporarily because of increasing cases of covid-19, but patients who have age factors such as women who are in the middle of an intervention in a treatment cycle or for fertility preservation before oncology treatment. Treatment cycles should be completed with full counselling and understanding of the patients [27]. Some recommendations that enhance the chance of acquiring the infection and help conserve the essential resource of healthcare workers of infertility treatment clinics show in Table 1.

Table 1: IVF protocol modifications pre-and post COVID-19 (Considerations on the restriction of ART due to COVID-19)

IVF Protocol Modifications	
Pre COVID-19	Post COVID-19
In-person consultations	Telemedicine consultations
In-person meetings with nurses, coordinators	Virtual meetings with nurses, coordinators.
Unrestricted travel with no personal protective equipment	All staff were issued and encouraged to wear masks on their way to and from the centre, all patients were issued masks to wear at the centre if they didn't already have one.
Hepatitis B, C, HIV, and syphilis tests before stimulation	Consider the addition of SARS CoV-2 testing before the start of stimulation (if positive, do not start).
Multiple visits during stimulation (typically 5-7 visits before egg retrieval)	Space out visits during stimulation where appropriate (3-4 visits before egg retrieval). Temperature checks at each visit (patients and staff).
Crowded waiting rooms	Patients immediately roomed after checking in. Vital signs and blood draw were done while in the exam room. Seating and location of staff were changed to maintain >6-foot distancing wherever possible.
Rapid turnover of the ultrasound examination room	Empty waiting room, thoroughly wipe down surfaces, longer interval between procedures.
Partner encouraged to accompany the patient at visits, egg retrieval, and transfer	No partners or visitors (encourage the use of video-telephone products).
Sperm production on-site in the small collection room	Off-site sperm production.
Signed consent forms – common pens	Electronic consent forms-clean pens available if need to sign forms.

Both patients and health care workers should carefully check for body temperature and health status when they enter the clinic. Because of inadequate data regarding the impact of covid-19 on pregnancy and fetus, complete cessation of programs that include embryo transfer

whether fresh or frozen is done. The women, who have already started an ovulation induction segment for IVF should be taken care of. This treatment cannot be prolonged and should continue just for a single cycle. Oocyte should go for the freeze all method if retrieval

has already been planned and cryopreserve all gametes or embryos [28]. The guidelines of ESHRE (European society of human reproduction and embryology) should be followed by all the fertility laboratories. All the fertility care teams should be protective in providing emotional and psychological support not only to patients but also to all staff members and also arrange teleconsultations for patients and staff. Patients should avoid going to fertility centres for non-emergency procedures like egg donation, gestational surgery, etc. All the appointments with patients should be done in such a way that will complete all needed work in a single visit. Special care must be taken to disinfect vaginal probes, which are used during ovarian stimulation and oocyte retrieval [29].

All the medical specialties including hospitals and emergency departments are also challenged by Covid-19, which is trying to provide safe and essential care for fertility treatments. Implementation with low-cost IVF, EMI, and low-interest loans may cut short the financial burden to some extent-said doctor Dr Nitin marketing director of Indira IVF. To face this pandemic all the medical fraternity has started resuming medical care under restrict vigilance and precautions. A suggested patient entry only by appointment has been the norm, and the staff, clinic, and patients have been monitored for stringent sanitization and other precautions like PPE kits, masks, and shields etc [30,31]. Laboratories have been sanitized and embryology staff has been particular about sanitizing to rule out any possibility of contamination in the embryology laboratories. The staff has been given more priority in wearing protection uniforms than regular work uniforms. After every patient visit, the clinics are disinfected to rule any infection [32].

Dr Tanu of Indira IVF infertility treatment centre Jaipur tells about the precaution and ways for infertility treatment during this pandemic. For covid-19 testing, their lab followed the protocol in which the testing usually has preferred to do before the stimulation and even before pickup egg retrieval. The eggs can be cryopreserved and be saved for months to years without getting affected. The staff is taking proper precautions like sterilization of Operation Theater regularly, using masks, gloves, and PPE kit properly so health care workers don't need to be at risk. The SARS covid-19 virus or the coronavirus exhibited strong features of surviving in the air for several hours and even at usual laboratory

temperatures of about 22 degrees so special attention should be given to air quality control, including the use of air filtration systems and air pressurization particularly in surgical and laboratory areas [33]. This enhances the chance of survival of the virus and can affect the preserved eggs or contaminate the eggs or embryos. So doctors advise clinics to reevaluate and change the clinic temperature and pressures to ensure the complete absence of the virus. As the virus can stay in plastic for about 72 hours doctors are working around using quality-controlled covid-19 free culture dishes. Embryologists are encouraging to follow standard practices in IVF laboratories for infection control prevention. Such practices include the cleaning of supply boxes and gas cylinders before entering the laboratory using approved agents [34, 35]. The aim of these suggestions and changes during this pandemic of Covid-19 is to mitigate risk for patients, physicians, nurses, providers, laboratory and clinical staff, and the community and enhance critically needed resource conservation. With the unlocking phase, things have slowly started coming back to normal. Plans of couples, who were looking for treatment, need not be delayed anymore. All procedures of IVF are practised after initial risk assessment with covid-19 risk mitigation steps in a highly sanitized environment. There is no need to fear its success if we follow prevention guidelines issued by the government.

Practical contemplation for ART health professionals-

We should continue to look critically and dispassionately at the COVID-19 pandemic during the coming weeks. Our recommendations are unlikely to create any further burden to the medical infrastructure as ART in the population mentioned above is virtually free of complications. It has been realized that much is unknown about the implications of COVID-19 for early and late pregnancy, including maternal-fetal transmission and teratogenicity [36,37]. However, pregnancy can act as co-morbidity, and, therefore, it is currently recommended against conception by ART in most cases. However, it should also be acknowledged that new serology testing is being developed to help identify individuals who have had the infection and have recovered, suggesting that those people are now immune to the virus and could be allowed IVF treatment [38]. There will be less risk of recommencing care, particularly in COVID-19 recovered patients as IVF health care professionals recover from

COVID-19 infections and acquire immunity. Immune patients will have a low risk of pregnancy complications in the event of an embryo transfer, or of propagating the disease when attending a medical facility along these lines. After the debate on the accuracy of these tests, it is still unclear how long any immunity lasts and if reinfection is possible [39] and given the probability that this pandemic will continue for many months ahead we must keep an open mind, and look for what is and not for fear of what might be.

Myths about IVF during COVID-19- This covid-19 pandemic disrupted tens of thousands of IVF cycles. The late spring and early summer shutdown periods were one of great fear and uncertainty infertility circles and general trepidation about entering health care facilities. Now in recent times, fertility issues have risen amongst couples of all ages they are choosing medical help to become parents but because of the severity of this pandemic, several myths are originating in becoming parents as follows [40].

Infection or vaccines affect fertility: Dr says there is no proof to show this myth, would-be moms getting IVF treatment needs to be tested before the treatment process if tested positive gets cancelled. **Covid vaccines aren't safe during IVF treatment:** Because of this myth women are away from vaccines while undergoing IVF treatment. Medical organizations have confirmed the approved vaccines safely for those taking the treatment.

Due to the ongoing pandemic, there has been a delay in IVF treatment: Many would-be parents assume, it is better to delay the treatment in the current scenario but most reputed IVF centres follow rigorous safety measures to ensure successful treatment and most reproductive age patients are not in high risk and should not avoid delay. **Pregnancy is affected by coronavirus:** This myth has acted most women, who have successfully got pregnant by IVF treatment. Dr says that the infection risk is the same for every woman, pregnant or not. It has also been scientifically that the infection does not pass to the children via the mother.

At the time of writing of this paper on June 6, 2021, as the vaccine rollout has spread across the country IVF clinics have hosted lots of talk about potential risks. Dr Amato says that several misstatements about vaccines and infertility, those vaccines causing fevers that could affect implantation but there remains controversy about

whether fevers can cause birth defects, although this effect has never been revealed by hard data [41].

CONCLUSIONS

A point of view is provided in this article that helps the health care providers to identify priorities and remedies for infertile patients impacted by the covid-19 pandemic. Fertility suspension during the covid-19 pandemic have had a considerable negative impact on couples mental health and quality of life, so several protective psychological factors are point out in the manuscript, that can be supportive in the future to help the infertility treatments. In a moment when preventing complications and limiting burdens for national health systems could still represent a relevant issue, the correct prognostic stratification of patients and the identification of more "time-sensitive" cases are crucial for guiding the gradual restart of ART services. Relevant Insights are provided from this review paper for competent authorities, healthcare providers and IVF centres, when developing, modifying, and implementer infertility treatment strategies during and after the covid-19 pandemic.

There is a need to develop clear and altered plans to ensure the ability to provide care with maximizing the safety of current regarding new medical findings in future and urgent awareness should be essential among canaille regarding the reproduction of health during this covid-19 pandemic era.

CONTRIBUTION OF AUTHORS

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