

Position Statement from ISAR

**Recommendations for
COVID Vaccination
During Fertility Treatments and
Early Pregnancy**



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Recommendations for COVID Vaccination During Fertility Treatments and Early Pregnancy

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KEY POINTS

1. All the available vaccines - Covishield or Covaxin or Sputnik-V can be used in both men and women contemplating pregnancy.
2. In men and women who receive the vaccine, it seems prudent to postpone assisted reproduction treatments for ONLY a few days after ADMINISTRATION of vaccine
3. In patients who have had COVID-19 disease and could have developed immunity, vaccination may be advised 12 weeks from infection or 4-8 weeks from recovery
4. Currently available data do not report a negative impact of COVID-19 vaccination during the periconceptional period and pregnant women should also have access to vaccination
5. COVID vaccine can be simultaneously administered along with other vaccines like tetanus and influenza DURING PREGNANCY but a 14-day interval between vaccines IS ADVISABLE



INTRODUCTION

As we mark the one-year anniversary of the declaration of COVID-19 as a global pandemic, it has become abundantly clear that this virus will not disappear soon. India is currently experiencing the second wave of the pandemic and is striving towards preparedness for an expected third wave. While COVID-19 norms of face masks, physical distancing and frequent hand sanitization are effective mitigation strategies, an increased awareness about quarantine following exposure and timely testing add to the value of above measures. However, vaccination plays an extremely important role in achieving herd immunity against this infection.¹ Compliance with the above measures will influence the regional prevalence of the disease and restrict it to an endemic in certain regions and we will need to learn to live with it. Despite a significant overall decrease in active cases of Covid, statewide positivity and transmission rates continue to differ in India.

Indian Society for Assisted Reproduction (ISAR) supports strict adherence to its earlier recommended COVID appropriate behaviour strategies such as masking, use of social distancing, and rigorous attention to hand washing, for disease prevention.² It also supports the use of triage for both patients and hospital staff, appropriate Personal Protective Equipment (PPE), implementation of travel restrictions and quarantines as indicated. ISAR acknowledges benefit of emotional support for women undergoing fertility treatments by their accompanying partners or support persons. However, currently such practices are discouraged.

The emotional and mental struggle which people experience due to pandemic fatigue, information overload, misinformation, loneliness, fear, confusion, and other psychological factors are being increasingly recognised. Patients are disappointed by the delays in treatment, additional steps such as multiple COVID-19 tests during treatment, and the inability of partner to attend the clinic with them. This may delay the situation from reaching the new-normal with COVID appropriate protocols and vaccination. Motivations, perceptions, and responsible behaviours of the patients will help fertility clinics develop successful strategies to ensure safe reproductive care. It is also important that reproductive care centers continue to ensure double masking, hand washing, avoidance of crowds, and physical distancing.

The following recommendations are developed based on the currently available and published evidence and relevant guidelines from Federation Obstetrics & Gynaecological Societies India (FOGSI), The International Federation of Gynecology and Obstetrics (FIGO), American Society for Reproductive Medicine (ASRM), European Society of Human Reproduction and Embryology (ESHRE), British Fertility Society (BFS) and Society for Male Reproduction and Urology (SMRU).



COVID-19 VACCINES

Many countries, including India have cleared one or more type/s of vaccine/s on an emergency basis for mass vaccination of the population. Currently available vaccines against Covid-19 contain one of the following: mRNA, adenovirus as vector and protein subunit. Available evidence shows that vaccination is effective against symptomatic and asymptomatic infection, hospitalization, severe-critical disease, and mortality. They are believed to be effective against the commonly encountered SARS-CoV-2 variants.^{1,3} However, concerns remain regarding their effectiveness against the increasingly changing variants with higher transmission rate and possibly higher mortality than seen in the first wave. The high transmissibility increases the percentage of the population required to achieve herd immunity, which can only be achieved with mass vaccination drive. Moreover, we must remember that India with a large population will take time to get the entire population vaccinated and thus herd immunity development. Common side effects after COVID-19 vaccination include fever, chills, fatigue, myalgia, and headaches, which typically occur and resolve within three days.

Covid-19 vaccines in India

There are three different vaccines against Covid available in India. They are Covishield incorporating a replication incompetent adenovirus vector; COVAXIN, a mRNA vaccine and Sputnik -V, an adenovirus vectored vaccine. Currently, the first two are manufactured within the country, and the third is imported from Russia. Central Drugs Standard Control Organisation (CDSCO) granted approval of restricted emergency use to Covishield and COVAXIN vaccines on 2nd January 2021. Further, permission for restricted use in emergency situations was granted for Sputnik-V vaccine by Drug Controller General of India (DCGI) on 13th April 2021. It is important to note that none of these vaccines contain live attenuated virus. Ministry of Health and Family Welfare (MoHFW) has introduced phased vaccination in the country since 16th January 2021 starting with frontline workers and elderly population and subsequently including younger population.⁴ All the above vaccines require two doses to be administered. Relevant information regarding the three vaccines are included in Table 1. It is important to note that while all of them have shown high efficacy in phase III trials, the effectiveness observed in population would be less than this, as seen previously with any mass vaccination programme. While they do not completely prevent COVID, their effectiveness in reducing the severity of disease and mortality are considered as important factors when creating this recommendation for administration of the vaccine to women who are pregnant or to couples attempting pregnancy.^{5,6}

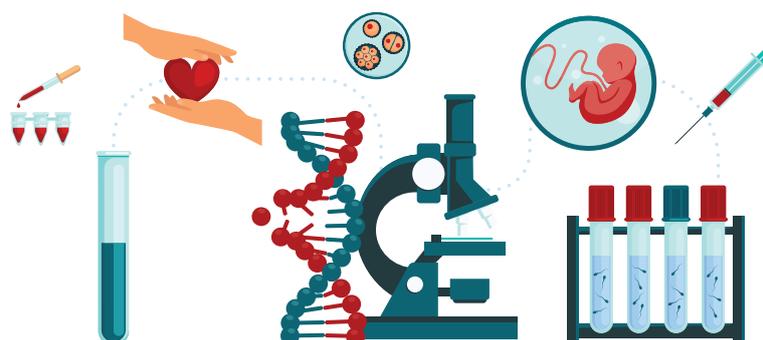




Table 1: Salient information on the currently available vaccines against COVID-19 in India

Vaccine	Manufacturer	Type	No. of doses	Time interval between doses	Efficacy* (Phase III trials)
Covishield	Asta Zeneca-Serum Institute of India	Adenovirus with Double stranded DNA	2	Min 28 days Recommended 12-16 weeks apart	82.4%
COVAXIN	Bharat Biotech	Inactivated coronavirus	2	4 weeks apart	80.6%
Sputnik V	Gamaleya	Adenovirus with double stranded DNA	2	3 weeks apart	91.6%

*Efficacy against severe illness and death may be higher than the overall documented efficacy.

COVID-19 VACCINATION FOR PEOPLE UNDERGOING / AWAITING FERTILITY TREATMENTS

Infertile couples are an important subgroup of population at risk of developing Covid-19 due to one or more of the following reasons:

1. Need for frequent travel to access treatment and hence increased risk of exposure
2. Largely not vaccinated at present as majority of them are under 45 years of age
3. Many have certain co-morbidities such as obesity, impaired glucose tolerance or diabetes mellitus, hypertension or autoimmune disorders. Women with PCOS constitute an important group at high risk of developing severe Covid-19.⁷
4. Possible misconceptions, and misinformation regarding safety of vaccine in pregnancy and consequent vaccine hesitancy.

Hence there is an urgent need for recommendations pertaining to vaccination for this population, to assist in engaging and encouraging them for vaccination. It should be acknowledged that availability of vaccines and evolving eligibility criteria for the entire adult population of the country need to be discussed during counselling the couple.



1. Impact of Vaccination on Fertility:

The concerns that Covid vaccinations may be associated with infertility are considered to be unfounded⁶. While fertility has not been specifically studied in the clinical trials of the vaccine, no loss of fertility has been reported among trial participants or among the millions who have received the vaccines since their authorization, and no evidence of infertility appeared in animal studies. Current evidence from a study in women undergoing consecutive IVF cycles before and after vaccination does not show any negative impact of vaccination on ovarian stimulation, oocyte or embryological parameters, in those who commenced treatment 7-85 days following vaccination.⁶ Hence, patients undergoing fertility treatment should be encouraged to receive vaccination as soon as they become eligible for vaccination in the national programme.

2. Vaccination strategy in men and women awaiting fertility treatments:

Women who are fully vaccinated may start their fertility treatment within a few days after the last dose (avoid COVID-19 vaccination at least three days prior and three days after their procedure). The treatments include any surgical procedures, oocyte retrievals, embryo transfers or intrauterine insemination. The short time interval is to allow for the immune reaction to settle in and to tide over any transient febrile reaction following vaccination.^{8,9} The side effects make it difficult to determine if a post-procedure fever is related to the vaccine or to a developing infection related to the procedure. Any anaesthesia administered may further affect the thermoregulation transiently.

Women who are at high risk of developing COVID-19 during the course of treatment or at a high risk of pregnancy related complications should be advised to prioritize vaccination before pregnancy.

However, it is recommended that as the accessibility improves, all women seeking fertility treatments should be counselled and encouraged to proceed with vaccination. An important dilemma that may arise is that whether pregnancy should be postponed until after the second dose is received. Even though there is no data to guide the clinical practice in this scenario, a balanced advice would be not to delay pregnancy in view of the safety of these vaccines in pregnancy (see below). This is of particular relevance to those women of advanced maternal age or with reduced ovarian reserve.¹⁰

Men who have completed vaccination may commence treatment and provide semen samples a few days after vaccination and a protracted wait is not necessary.⁹

Those who have had any allergic reaction to the vaccine should proceed with treatment upon such advice from the physician.

However, treatment should not be delayed to the couples while waiting for the availability of vaccine.



3. Time interval between vaccination and pregnancy:

Most data regarding the safety of vaccines is from animal studies or women who had taken vaccination unknowingly when pregnant. Since the vaccine is not a live virus, there is no reason to delay pregnancy attempts because of vaccination administration or to defer treatment until the second dose has been administered. The product information for the available vaccines states that ‘animal studies do not show any harmful effect in pregnancy’. There is a growing number of women receiving the vaccination during pregnancy.¹⁰ No specific time interval is considered necessary upon vaccination before attempting pregnancy.

4. Recent COVID-19 infection and vaccination:

Currently, it is known that, antibodies may be identified for up to six months or longer, following an infection with COVID-19.⁶ It is recommended that a physician’s opinion is sought prior to commencing any fertility treatment, in particular in those who needed hospitalization both regarding the timing of treatment and of vaccination. Nature of treatment and possible risk of thromboembolism (TE) thereof should be discussed with the physician. Vaccination may be advised 12 weeks from infection or 4-8 weeks from recovery.¹¹

5. Vaccination of pregnant women:

There is emerging data that demonstrate that pregnancy is a high-risk condition for the development of severe disease and increased mortality associated with COVID-19.¹² Both mother and the fetus are more vulnerable to COVID infection. Though the pregnant women were not included in the initial COVID-19 vaccine trials, the data of safety comes from women who received vaccination without being aware of their pregnancy. Pregnant women do not experience any more side-effects than their non-pregnant counterparts. Current evidence suggests that there is an increased risk of miscarriages, and preterm birth following COVID-19 during pregnancy.^{12,13}

There is compelling evidence that COVID-19 vaccines are being increasingly accepted during pregnancy.¹⁴ Currently, there is no specific recommendation to choose any one type of vaccine.¹⁵ However, it is important to note that there should be a gap of 14 days before and after vaccination against covid and any other vaccine/s routinely administered during pregnancy.¹⁵

A more detailed recommendation on COVID-19 vaccinations and pregnancy can be found at:

<https://www.fogsi.org/covid-vaccination-for-pregnant-bf-women/>

<https://www.figo.org/covid-19-vaccination-pregnant-and-breastfeeding-women>



VACCINATION HESITANCY

Vaccination hesitancy was reported to varying degrees from different geographic areas of India when the vaccination became available in the month of January 2021. Spread of misinformation led to a “wait and see” policy as to how the vaccine is working for others before getting vaccinated themselves. This has now decreased after the steep rise in the cases in April and May 2021 and the compliance is improving. Sharing of personal experiences by healthcare providers, especially by doctors and nurses who were first in taking the vaccine as COVID warriors, helps in building trust in vaccines. Other proven methods for improving vaccination rates include the use of automatically scheduled appointments, easy access to vaccination clinics, seamless arrangements at vaccination centres and provision of vaccines during extended hours.¹⁶

COVID-19 VACCINATION AND RECOMMENDATIONS FOR REPRODUCTIVE CARE PROVIDERS

- Most of the healthcare workers including those in fertility clinics are fully vaccinated by now in India. ART centres should prioritize vaccination of any new member of staff.
- This should be in combination with continued enforcement of COVID norms of face masks, avoiding crowd in the clinics, physical distancing, and screening.
- Reproductive care providers must acknowledge the existence of vaccine hesitancy in a proportion of our population, presence of misconceptions and lack of availability of vaccine to young population although this situation is improving rapidly.
- Reproductive health care provider must tailor vaccination discussions appropriately with all patients
- They must provide accurate information and suggest reliable sources of information about COVID safe and appropriate behaviour and vaccination.
- Acknowledge fears, anger, and other negative emotions
- Share personal experience and vaccination confidence.
- Serve as vaccine ambassadors and help promote vaccine utilization and combat vaccine hesitancy and misinformation, to facilitate the health and safety of our patients, our communities, and overall society.





SUMMARY RECOMMENDATIONS ON VACCINATION AND FERTILITY TREATMENT

- All the available vaccines - Covishield or Covaxin or Sputnik-V can be used in both men and women contemplating pregnancy.
- All patients contemplating pregnancy or are pregnant should have access to all available information about the safety and efficacy of the vaccines.
- In men and women who receive the vaccine, it seems prudent to postpone assisted reproduction treatments for at least a few days (ideally 3-4 days) after the completion of vaccination.
- In patients who have had COVID-19 disease and could have developed immunity, vaccination may be advised 12 weeks from infection or 4-8 weeks from recovery
- Currently available data do not report a negative impact of COVID-19 vaccination during the periconceptional period and pregnant women should also have access to vaccination
- COVID vaccine can be simultaneously administered along with other vaccines like tetanus and influenza during pregnancy but a 14-day interval between vaccines is recommended

CONCLUSION

Infection with COVID-19 can lead to ongoing illness across a wide array of organ systems after regression of disease. Some of the reported symptoms include fatigue, cognitive difficulties, pain, autonomic disturbances, anxiety, and depression. Long term effects on the respiratory, cardiac and nervous system has also been reported. Prevention strategies should continue to be of utmost importance, not only to prevent death from acute disease, but also to prevent long term complications and ailments that affect a significant percentage of individuals who contract COVID-19. Effective management of COVID-19 cases will depend on the success of vaccination campaigns and the attainment of herd immunity, the effect of variants on disease severity and spread, and the degree to which mitigation efforts are proposed and followed. The fertility clinics should monitor and compare the outcomes of assisted reproduction treatments in vaccinated versus non-vaccinated patients. This will help in providing data to assess the safety of vaccines for pregnant women and their offspring and guidance for future recommendations.



DISCLAIMER

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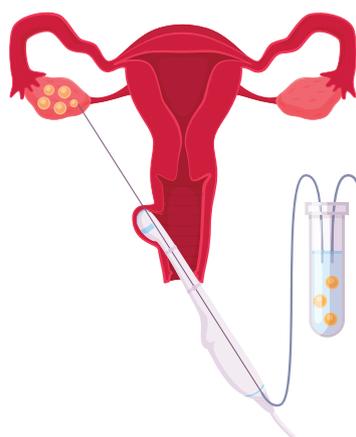
The advice expressed herein is not binding on professionals working in the field of human reproduction and embryology. Clinicians should always use their best clinical judgment in determining a course of action and be guided by the needs of the individual patient, available resources, and institutional or clinical practice limitations..

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