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Endometrial Evaluation and Infections in ART

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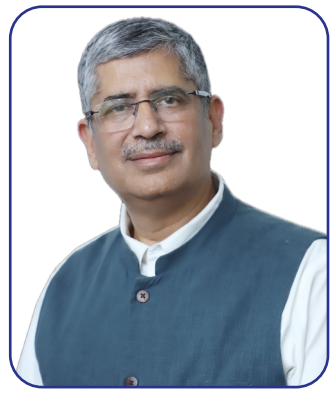
Message from the **President's Desk**



Dr Pankaj Talwar
President

Dear Friends,

It is indeed a pleasure to address you all on this issue of IFS Conversations. We look forward to seeing you all at Ahemdabad, from 6th to 8th Dec. 2024.

In this IFS conversation we have dealt with Infection in ART. The editorial team and the authors have worked very hard towards it. Hope you all will find it very useful. The conversation also showcase various recent academic activities conducted by our extremely enthusiastic and committed members of state chapters and Special interest groups.

Wishing you all a very pleasant reading of this issue of IFS Conversation!

Message from the **Secretary Desk**

Dr Shweta Mittal
Secretary General

Dear Friends,

Greetings from team IFS
IFS conversations is the official newsletter, this particular issue focuses on "Endometrial Evaluation and Infections in ART" in the fiield of Reproductive medicine and infertility. Hope all members enjoy reading and keeping them professionally updated.

Please go on to the IFS website and answer the surveys we have put in for pan India data collection We look forward to seeing you participate actively in Fertivision 2024 at Ahemdabad where you would see IFS at its best – academically, socially and culturally bringing together global and national leaders in the field and please go through the iterature published by IFS. Do not miss it!

Message from the **Editor's Desk**

Dr Rupali Bassi Goyal
Editor

Dear Friends,

Greetings from team IFS
We are pleased to release this edition of IFS Conversations which is based on theme "Endometrial Evaluation and Infections in ART" It specially covers interviews of Lifetime awardees, President and Gen. Sec.

We sincerely thank all our authors for their wholehearted contribution towards this issue of IFS conversation. We would love to hear your comments and suggestions and encourage all our readers to contribute in our forth-coming issues of IFS conversations.

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Invited Articles

Genital TB - An Update of current scenario

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Introduction

Tuberculosis (TB) affects about 10 million people each year worldwide.[1] Mycobacterium tuberculosis typically affects lungs, though extrapulmonary TB (EPTB) involving lymph nodes, bones, joints, meninges and urogenital tract can also occur.

One of the types of EPTB is female genital TB (FGTB), responsible for 9% cases of EPTB. FGTB usually affects young females, causing infertility, chronic pelvic pain, menstrual abnormalities, dyspareunia and chronic pelvic inflammatory disease.

The bacilli spread to genital tract occurs through hematogenous route, lymphatic spread, and contagious spread from gastrointestinal TB or rarely from an infected male partner through sexual transmission. Advanced disease causes permanent damage to endometrium and fallopian tubes and so earlier the diagnosis, better is the prognosis.[2]

Epidemiology

In infertility patients, incidence of FGTB varies from 3 to 16 % in India with higher incidence in tertiary referral centres. From a study from AIIMS, New Delhi, the incidence of FGTB in women with infertility was 26% and incidence of infertility in FGTB cases was 42.5%.[3] Also, the incidence was 24.5 % in women seeking assisted reproduction and was higher (48.5%) in women with tubal factor infertility.[4]

Etiopathogenesis

In most of the cases, FGTB is caused by Mycobacterium tuberculosis. Rarely, other organisms like Mycobacterium bovis can also be responsible.[5]

The fallopian tubes are the most common structure involved in FGTB, being affected in 90-100 % of the cases, and usually being bilateral. TB salpingitis can be endosalpingitis, exosalpingitis, interstitial tuberculous salpingitis and salpingitis isthmica nodosa. In cases with endosalpingitis, the fimbriae leading to hydrosalpinx or pyosalpinx formation may get blocked. Tubo-ovarian mass formation can also occur.[5]

Involvement of endometrium occurs in 50–80% of the cases and is an important cause of intrauterine adhesions (Asherman's syndrome causing secondary amenorrhoea and infertility, which is very difficult to treat.

Involvement of ovaries occurs in 20%–30% of cases, with findings of adhesions, caseation, adnexal cysts, tubo-ovarian masses, and diminished ovarian reserve. Involvement of the cervix (5%–15% of cases), or the vagina or vulva (1%–2%) is rare.[6] Cervical TB may mimic cervical cancer and present with abnormal vaginal discharge.[7] Vulval TB may present as hypertrophy or vulval tumor and vaginal TB may present with a fistula.[2]

Symptomatology[5]

About 10-120% women maybe asymptomatic and show no obvious sign of tuberculosis. The clinical features vary according to organ of involvement. Most commonly, patients present with infertility or menstrual disturbances like abnormal uterine bleeding in early cases to hypomenorrhoea and amenorrhoea when endometrium is damanged. Constitutional symptoms like fever, weight loss, malaise, anorexia, night sweats and generalised feeling of unwellness maybe present. Vague abdominal pain or pelvic pain, abnormal vaginal discharge or abdominal distention can occur. Symptoms of TB at other sites such as cough, sputum, hemoptysis or chest pain like in cases of pulmonary TB should always be asked for. Rarely, patients may present with acute abdominal pain due to rupture of abscess or flare up of lesions after some procedure.

On examination, some patients maybe absolutely normal and show no sign. Pallor maybe present on general examination. A through systemic examination should be carried which may reveal lymphadenopathy, rales on chest auscultation, swollen and inflammed joints with or without discharge, abdominal distension and ascites. Local examination may show enlarged Bartholin or growth/ulcer on vulva (vulval TB), growth/ swelling in vagina (vaginal TB), cervical growth or ulcer (cervical TB), abnormal vaginal discharge, enlarged uterus and pus discharge from cervix in case of pyometra, unilateral or bilateral tubo-ovarian masses and tenderness. Rarely rectovaginal or vesicovaginal fistula maybe present.

Diagnosis

As in early cases of FGTB, the patient maybe asymptomatic and hence a high level of suspicion should be kept especially in women presenting with infertility, secondary amneorrhoea and tubovarian masses.

A battery of investigations can be done to diagnose FGTB.[8] In suspected cases, a basic hemogram with ESR should be done which can reveal lymphocytosis with raised ESR. Serum CA-125 levels of >35 IU/L maybe seen in FGTB, though it is non specific. Mantoux test positive with value >10 mm may give some clue. Chest x-ray is one of the first line investigations advised and it may show old healed or active tubercular lesions. Endometrial aspiration or biopsy or peritoneal or lesion biopsy is one of the most important investigation. The various tests which can be done on it are AFB microscopy, AFB culture, Cartridge-based nucleic acid amplification test (CBNAAT) or gene Xpert, PCR (polymerase chain reaction, histopathology for epitheliod granuloma and newer molecular tests like Xpert ultra, TB- LAMP.[9][10]

Some radiological investigations can give indirect evidence of FGTB. Hysterosalpingography (HSG) is an investigation commonly done in infertile women mostly to diagnose patency of fallopian tubes. It should not be in cases of active FGTB as it can lead to sudden flare and spread of TB to peritoneum. Various findings of FGTB on HSG can be blocked tubes (usually cornual block), tobacco-pouch appearance of tubes, beaded tubes, hydrosalpinx due to fimbrial block (Fig 1), filling defects in uterine cavity (Asherman's syndrome).[11] Ultrasound, especially TVS is useful in diagnosing hydrosalpinx which shows cogwheel appearance with tubal dilatation with septae due to tubal mucosal thickening. In cases of suspected asherman's syndrome 3D/4D USG can be used for endometrial cavity evaluation. Loculated ascites and tubo-ovarian masses may also be seen on USG. CT and MRI also may depict hydrosalpinx or pyosalpinx, tubo-ovarian abscesses, ascites, peritoneal deposits, lymphadenopathy, and/or lesions in other abdominal viscera. PET-CT may show non-specific uptake in the tubo-ovarian masses.[12]

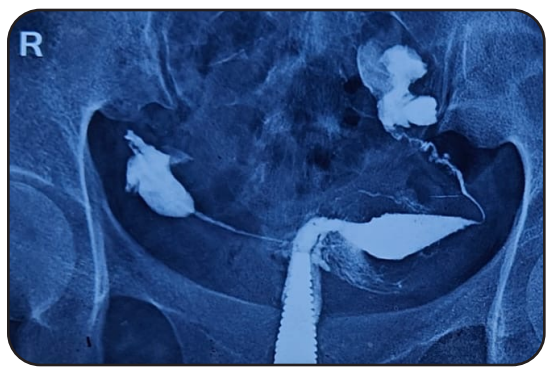

Fig 1: HSG showing hydrosalpinx due to fimbrial block

Laparoscopy and hysteroscopy are valuable in investigating the cases of infertility and FGTB. Various signs have been described in cases of abdominopelvic TB like perihepatic adhesions (Fitz-Hugh-Curtis)with Sharma's hanging gallbladder, Sharma's ascending colon adhesion, Sharma's sigmoid colonic adhesive band, Sharma's compartmentalization sign in abdomino-pelvic TB (multiple compartments are formed by omental adhesions to contain infection), Sharma's parachute sign with ascending colon being adherent to anterior abdominal wall.[13][14] In some cases fallopian tubes are distended with alternate constrictions and dilatations on laparoscopy and dye test resembling blue python (Sharma's blue python sign) is seen (Fig 2). Fusion of both fallopian tubes due to FGTB (Sharma's kissing fallopian tubes sign) has also been observed.

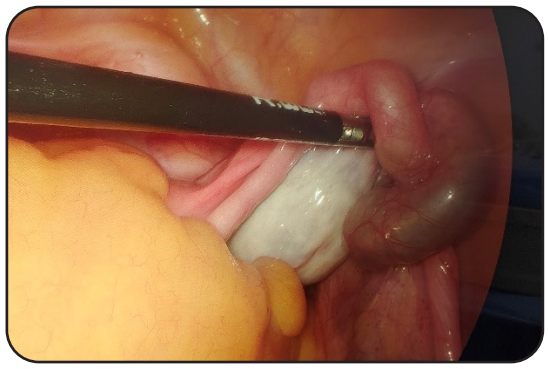

Fig 2: Sharma's Blue python sign

On hysteroscopy various TB lesions seen are pale endometrium, tubercles, caseous nodules, chronic endometritis, edema, micropolyps, varying grades of intrauterine adhesions and distorted and shrunken uterine cavity with obliterated ostia.

In the absence of availability of any single sensitive and specific test for detection of FGTB, combination of tests can be used to increase the sensitivity and detection rate of FGTB. The tests which are suggestive of definitive diagnosis of FGTB are positive AFB microscopy, culture, CBNAAT or Gene-xpert positive and epitheliod granulomas on endometrial biopsy. In cases where PCR is positive, additional investigations like diagnostic laparoscopy and radiological investigations like HSG, TVS, CT/MRI and PET-CT can be used for confirming the diagnosis.[5]

Medical treatment

Treatment should preferably be directly observed treatment short course (DOTS) with quality assured free medicines from government DOTS centers present all over India under National TB Elimination program (previously called Revised National TB Control Program).

The treatment of FGTB is same as that of pulmonary TB. Total treatment duration is 6 months with 2 months of intensive phase and 4 months of continuation phase. There are 4 drugs, Isoniazide (H), Rifampicin (R), Pyrazinamide (Z), Ethambutol (E) given in intensive phase daily for 2 months. In the continuation phase, 3 drugs (unlike 2 drugs in past) Isoniazide (H), Rifampicin (R) and Ethambutol (E) are given daily over a period of 4 months. In the case of drug-sensitive TB, even patients with irregular treatment or defaulters are treated with the above regimen only. The category system is no longer used. The doses are as per weight bands and are given below in Table 1.

Table: 1
Drug treatment of drug-sensitive and isoniazid-resistant FGTB as per WHO and National TB Elimination Program (NTEP)[15]

Drug-sensitive FGTB (rifampicin- and isoniazid-sensitive new, previously treated, or retreatment TB cases)

Daily dose regimen for adults as per weight bands

Number of tablets of fixed drug combination (FDC)

Weight category	Intensive-phase HRZE 75 mg /150 mg/400 mg/275 mg Per FDC tablet (2 months) oral daily treatment	Continuation-phase HRE 75 mg /150 mg/275 mg per FDC tablet (4 months) oral daily treatment	Streptomycin* (g)
25–39 kg	2	2	0.5
40-54 kg	3	3	0.75
55-69 kg	4	4	1
≥ 70 kg	5	5	1

*Streptomycin is given only for adverse drug reaction to first-line drugs like drug-induced hepatitis when HRZ are withheld and streptomycin, ethambutol and levofloxacin are given till liver function tests (LFT) return to normal, when RHZ are added sequentially under LFT monitoring

Surgical Treatment in FGTB (5)

There are limited indications of surgery eg. drainage of abscesses. Surgery in cases of TB is difficult and best avoided. However, diagnostic laparoscopy and hysteroscopy can be done at beginning to diagnose the disease and later after completion of full treatment of TB to prognosticate the patient and to plan further treatment for infertility.

Conclusion

In young females, FGTB is an important cause of reproductive and genital morbidity causing infertility in developed countries. Diagnosis at times is difficult and concomitant use of various tests and algorithm for diagnosis and management should be followed. Following early diagnosis and treatment, the prognosis is better. The treatment is same as that of pulmonary TB and directly observed treatment short course (DOTS) as described above should be used.

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Effectiveness of Immunomodulation in ART- What evidence says?

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Immunomodulation play a pivotal role in assisted reproductive technologies (ART), particularly in cases where immunological factors contribute to infertility or implantation failure. Immunomodulators help to modulate these immune responses to support embryo implantation and fetal development by:

1. Regulation of Immune Responses in Pregnancy

- Pregnancy is a delicate immune balance where the maternal immune system must tolerate the semi-allogeneic fetus.
- Immunological dysregulation, such as excessive activation of natural killer (NK) cells or an imbalanced Th1/Th2 cytokine ratio, can lead to recurrent implantation failure (RIF) or recurrent pregnancy loss (RPL).

2. Treatment of Autoimmune Disorders

- Autoimmune conditions like antiphospholipid syndrome or thyroid autoimmunity can impact implantation and pregnancy outcomes.
- Immunomodulators, such as corticosteroids, hCG or intravenous immunoglobulins (IVIG), suppress autoantibodies and inflammation, improves pregnancy rates in affected women.

3. Reduction of Inflammation

- Chronic endometritis and other inflammatory conditions of the reproductive tract can interfere with endometrial receptivity.
- Immunomodulators like antibiotics (for infection-induced inflammation) or low-dose aspirin improves uterine blood flow, hence help to mitigate these effects, enhancing the chances of successful implantation.

4. Enhancing Endometrial Receptivity

- An immunologically conducive endometrium is essential for embryo implantation.
- Immunomodulatory strategies, such as the use of hCG, granulocyte-colony stimulating factor (G-CSF), intralipid or peripheral blood mononuclear cells (MOA) can promote endometrial receptivity and increase implantation rates. Peripheral blood mononuclear cells may be very promising as it Improves implantation by raising endometrial levels of LIF and VEGF. PBMCs after activation by hCG, increase matrix metallopeptidase-2 (MMP-2), MMP-9, and VEGF and hence, stimulates trophoblast invasion.

5. Preventing Rejection of the Embryo

In cases of alloimmune rejection, immunomodulators like IVIG, low-molecular-weight heparin (LMWH), or TNF-alpha inhibitors can prevent rejection and improve pregnancy outcomes.

6. Role in Recurrent Implantation Failure (RIF)

- In cases of unexplained RIF may be involved by subtle immune dysfunctions.
- Immunomodulators, including corticosteroids, intra lipid, platelets rich plasma, IVIG, and leukocyte immunization, may be required to address these issues and improve ART success rates.

Commonly Used Immunomodulators in ART

- Corticosteroids (e.g., prednisone): Suppress overactive immune responses.
- Intravenous Immunoglobulin (IVIG): Modulates antibody-mediated immunity and reduces NK cell activity.
- Low-Molecular-Weight Heparin (LMWH): Has anticoagulant and immunomodulatory effects.
- Low dose hCG: Has a strong immunomodulatory effect and increases the endometrial angiogenesis.
- Granulocyte-Colony Stimulating Factor (G-CSF): Enhances endometrial receptivity.
- TNF-alpha inhibitors: Address elevated inflammatory cytokines in specific cases.
- Platelets Rich Plasma: Interleukins and growth factors play a crucial role in implantation. It decreases the plasma levels of inflammatory cells and increases GF.
- Peripheral blood mononuclear cells (MOA): Improves implantation by enhancing endometrial levels of LIF and VEGF.

Conclusions

Immunomodulators seems to be essential in ART program for addressing immune-related infertility issues, improving implantation rates, and reducing the risk of miscarriage. Their judicious use, guided by detailed immunological assessments, can significantly enhance the success of assisted reproduction. But it should be considered by:

i. Individualization of treatment: The use of immunomodulators must be tailored to each patient's immune profile and clinical condition.
ii. Limited evidence in some cases: While some studies support the use of immunomodulators in ART, further research is needed to standardize their application and clarify their mechanisms.
iii. Potential side effects: Some immunomodulators, like corticosteroids, Intralipid can have systemic effects, necessitating careful monitoring.

The Role of EMMA and ALICE in Infertility: A Comprehensive Analysis

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The Human Microbiome Project has highlighted the importance of micro- organisms and their genomes in entire body. Furthermore it was analysed that approximately 9% of the total human microbiome is found in the female reproductive tract[1]

It is now a well established fact that the endometrial and the vaginal microbiota vary markedly. Indeed the variation in the endometrial microbiota with increasing maternal age has also been demonstrated by a Japanese study. In this the author demonstrated a decrease in lactobacillus quantity with the endometrial becoming pre receptive with increasing age.[2]

In the female reproductive tract Lactobacillus spp. are the most frequently identified bacteria. An NGS (next-generation sequencing) analyses of the V3–V4–V6 regions in the 16S rRNA revealed that the endometrial microbiome comprises low-biomass microbiota as well as lesser in numbers as compared to the vaginal flora[3]

There have been multiple studies to prove the association between the presence of bacterial chronic endometritis (CE) and persistent inflammation of the endometrial mucosa. This further leads to an impaired endometrial receptivity through alterations of decidualization and various cellular mechanisms.[4]
Moreno et al , conducted a multicentre prospective study in which he observed that implantation failure was associated with the depletion of Lactobacillus. [5]

Endometrial Receptivity Analysis (ERA)

Endometrial receptivity analysis (ERA, Igenomix) is the a commercial test available for clinical investigation. This test utilizes an assay of 248 genes expression patterns of to identify the receptivity status (receptive or non-rreceptive) of the endometrium. This further helps in determining the window of implantation displacement in a specific patient.[6]

According to a recent systematic review and meta-analysis by Liu etal[7] the window of implantation would be displaced in as high as one?third of infertile women. In patients with recurrent implantation failure a personalized embryo transfer based o the receptivity assay would facilitate implantation.[7]

EMMA

Endometrial Microbiome and Metagenomic Analysis

EMMA analyses the endometrial microbiota and its relationship with fertility, implantation, and pregnancy outcomes. EMMA guides by examining the endometrial microbiome favourable for successful implantation and pregnancy outcomes. It helps in tailoring personalized approach for implantation.

Endometrial Preparation

Endometrial preparation with estrogen is to be given by oral or transdermal routes etc. Once the endometrium, thickness reaches beyond 7mm, usually around the 12th day of the menstrual cycle , Progesterone may be started in the form of micronized progesterone 400mgs by vaginal route for approximately 120 hrs before the endometrial sample is taken.

Edometrial biopsy was performed using a biopsy curette, usually a Pipelle. The aspirated tissues (excluding mucus and blood) are placed into a cryotube containing RNA later (Qiagen), then stored and shipped at 4°C to be transported to the laboratory, in accordance with the manufacturer's protocol

Processing and Analysis

25 mg of endometrial tissue is treated with proteinase K at 56°C for 3 h, then separated and lysed with ATL buffer (Qiagen). Subsequently, the tissues are disrupted with a Tissue Lyser LT (Qiagen) for 5 min at 50 Hz using stainless steel beads. Bacterial nucleic acids from the sample were purified using QI Asymphony (Qiagen), in accordance.

Hypervariable regions of the gene encoding the bacterial 16S ribosomal subunit (V2–4–8 and V3–6, 7–9) are amplified using an Ion 16S metagenomics kit (Thermo Fisher Scientific). The amplified products are fragmented and barcoded with an Ion Plus Fragment Library kit and Ion Xpress Barcode Adaptors (Thermo Fisher Scientific), in accordance with the manufacturer's instructions. The individual libraries are pooled, and the emulsion polymerase chain reaction is performed using an Ion OneTouch 2 System or an Ion Chef System. Libraries are sequenced with the Ion Torrent S5 XL NGS system (Thermo Fisher Scientific)

Interpretation of EMMA

EMMA results were interpreted as
Pattern 1: Normal microbiome with Lactobacillus > 90% and negative for bacterial pathogens

Pattern 2: Abnormal microbiome with Lactobacillus < 90% and negative for bacterial pathogens causing CE (differed according to whether bacterial pathogens causing CE were present).

Pattern 3: Abnormal microbiome with Lactobacillus < 90% and positive for bacterial pathogens causing CE (differed according to whether bacterial pathogens causing CE were present)

Pattern 4: Mild dysbiotic microbiome profile (only trace amounts of bacterial DNA were detected)
Pattern 5- Microbiome with ultralow biomass.(no amplification of bacterial DNA (equivalent to the negative control containing only water).

ALICE
Analysis of infectious chronic endometritis

A tool that looks into the composition and operation of the endometrial microbiome is called ALICE, it provides a more Comprehensive Microbial Analysis of the endometrial microbiome. Identifying the specific microbiomes and directed treatment helps in guiding the directed therapy susceptible to a specific organism.

Interpretation of ALICE

ALICE were interpreted as positive when bacterial pathogens causing CE were present, as represented by pattern 3 in the EMMA results. Pathogens causing CE included Escherichia, Klebsiella, Enterococcus, Chlamydia, Mycoplasma, Ureaplasma, Streptococcus, and Staphylococcu

The Integration of EMMA and ALICE in Clinical Practice

Comprehensive Fertility Assessment
The combination of EMMA and ALICE offers a holistic approach to fertility assessment. By analyzing both the microbial composition and functionality, clinicians gain a thorough understanding of a patient's reproductive health. This comprehensive assessment is invaluable for identifying underlying causes of infertility that may have been overlooked in traditional evaluations.

Evidence-Based Treatment Protocols
Using the insights from EMMA and ALICE, fertility specialists can develop evidence-based treatment protocols. These protocols can incorporate dietary recommendations, probiotic therapies, and customized ART approaches, all tailored to the individual's microbiome profile. Such personalized strategies are more likely to yield positive outcomes.

Monitoring and Follow-Up
Continuous monitoring of the endometrial microbiome throughout the fertility treatment process is essential. EMMA and ALICE allow for periodic assessments, enabling clinicians to adjust treatment plans based on real-time data. This adaptive approach can enhance success rates and provide better support for patients.

Challenges and Considerations

Standardization of Protocols
One of the main challenges in integrating EMMA and ALICE into clinical practice is the need for standardized protocols. As these technologies are relatively new, establishing universally accepted guidelines for their use is crucial for ensuring

consistent and reliable results.

Patient Education and Awareness
Educating patients about the role of the endometrial microbiome in fertility is vital. Many individuals may be unaware of how their microbiome can impact their reproductive health. Increasing awareness can empower patients to make informed decisions about their treatment options.

Ethical and Privacy Concerns
As with any technology that involves genetic and microbiome data, ethical and privacy concerns arise. Ensuring that patient data is protected and used responsibly is paramount in maintaining trust and transparency in fertility treatments.

Contributing to Research and Development
ALICE plays a pivotal role in advancing research in reproductive health. By generating data on the endometrial microbiome, it opens new avenues for understanding the complex interactions between microbial communities and reproductive processes. This research can lead to the development of innovative therapeutic strategies to address infertility.

Literature review
There is paucity of data specifically directed towards EMMA and ALICE. Fuji et al in a recent study tried to analyse the Age and endometrial microbiota; related delay in development of endometrial receptivity. He studied the endometrial samples of 185 patients with endometrial trio (EMMA, ERA and ALICE) and cocluded that with advancing age there was a decrease in Lactobacillus-dominant microbiota; He further also concluded that with aging and endometrial microbiota with ultralow biomass were significantly associated with pre-receptive endometrium.[2]

Another single centre study which Compared the results of conventional endometrial biopsy pathology for chronic endometritis (CE) to commercially available endometrial microbiome testing (EMMA/ALICE, iGenomix), and correlation to embryo transfer outcomes. A retrospective analysis of 446 patients was performed and Clinical outcomes before and after EMMA /ALICE testing were done they found no concurrence between EMMA/ALIC testing and traditional pathology results. Amongst the patients with failed transfer the, subsequent FET outcomes were similar regardless if CE was detected and treated, or if no CE was detected by EMMA/ALICE. They also observed that in the subgroup of patients who had not had a prior FET, a normal EMMA/ALICE result was associated with increased live birth rate as compared to those with abnormal results.

Conclusion

Endometrial dysbiosis is an important factor in recurrent implantation failure. There is a paucity of literature on EMMA and Alice and further larger trials need to be done before they can be recommended routinely for patients undergoing ART procedures.

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The Impact of Sexually Transmitted Diseases on Female Fertility

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Introduction

Millions of women worldwide are affected every year by sexually transmitted diseases (STDs) posing a significant global health concern. According to the World Health Organization, more than 1 million sexually transmitted infections (STIs) are acquired daily worldwide, with a considerable proportion affecting women of reproductive age.[1] STDs like chlamydia, gonorrhea, human papillomavirus (HPV), herpes simplex virus (HSV), and syphilis contribute to a range of reproductive health issues. The potential threat to fertility is one of the most profound impacts of STDs on women, often through mechanisms that are not immediately symptomatic and therefore may go untreated.

This review examines the latest research on the association between STDs and female fertility, the mechanisms involved, the potential outcomes of untreated infections, and preventive strategies.

Mechanisms of STD Impact on Female Fertility

STDs do not spare the organs of reproduction, and the inflammation, scarring and damage to body tissues as a result can interfere with fertility. Chlamydia trachomatis and Neisseria gonorrhoeae are very particular, often left unnoticed and advancing silently, reproductive organs can suffer great destruction before one is diagnosed with such an infection.

Chlamydia, the second most commonly reported sexually transmitted infection in America, is typically "silent" in its presentation; about 70 to 90 percent of women who are infected do not exhibit primary symptoms.[2] However, if undiagnosed and unattended, such infections may lead to pelvic inflammatory disease (PID), a significant factor responsible for infertility, ectopic pregnancies, and chronic pelvic pain.[3]

HPV has a less direct effect on infertility and its primary mechanism is through damage to cervical tissue which, if not treated, may develop into carcinoma. Cervical function is important for reproductive health; however, HPV IV strains that are resistant and invade the cervix and require surgical procedures, like LEEP technique or cone biopsy, may be damaging to the cervical function further leading to reproduction failure or pregnancy problems.[4] While less common, factors like syphilis and HSV may not be directly causing infertility but are involved in pregnancy outcomes in the sense that these factors may increase the changes of miscarriage or preterm births.[5]

STD-Associated Inflammatory Conditions and Fertility

Pelvic inflammatory disease (PID) is one of the most serious sequelae of STDs that have not been addressed, especially chlamydia and gonorrhea. PID occurs as a result of pathogenic microorganisms that move from the cervix to the upper reproductive tract causing inflammation of the uterus, fallopian tubes and ovaries. Research shows that up to 10-15 percent of women who have chronic chlamydia or gonorrhea infections who are not treated develop PID and about 10-20 percent of those cases are infertile due to tubal scarring and adhesions.[6]

Women who experience PID claim tubal-factor infertility as the a tubal-factor infertility is very common among women with PID, because the fallopian tubes sustained within the range of an inflammation and fibrous tissue. This type of damage obstructs the passage of ova from the ovaries to the uterus making the procedure of getting pregnant complicated. Most importantly, the spermatozoa because of their partial tubal blockage have tendency to ectopic pregnancy[7] when they encounter such partial tubal blockage. As Torrone et al. noted in 2018, around PID was the cause of infertility among 4.2% of women within the age group 18 to 44 years living in the USA. These findings also point out the ubiquity of the condition and how it affects individuals during their reproductive life.[8]

Long-Term Fertility Implications of Untreated STDs

The progression of untreated STDs often leads to compounded health challenges over time. One study found that women with untreated chlamydia are 2-3 times more likely to suffer from infertility, ectopic pregnancies, or chronic pelvic pain than those who receive timely treatment.[9] Moreover, evidence suggests that repeated episodes of STDs, even if treated, can exacerbate reproductive damage. Reinfection with chlamydia, for example, increases the likelihood of PID by nearly 20%, further elevating infertility risks.[10]

A 2020 longitudinal study examined 15 years of data on women with untreated STDs, concluding that delayed treatment is a primary predictor of reproductive health complications, especially infertility. The authors emphasized that women who delay or forego STD treatment due to lack of symptoms or healthcare access are at heightened risk for irreversible fertility impairment.[11]

Screening, Prevention, and Early Intervention

While the best option is to practice safe sex, in the event of an STD, preventive screening and early intervention can significantly minimize any negative consequences such STDs can have on clinical fertility. As per the guidelines from the Centers for Disease Control and Prevention (CDC), younger women under 25 years of age who are sexually active should be screened for chlamydia and gonorrhea once a year, as well women over 25 who have a new or more than one recent partner[12] This helps to halt the spread of STDs metastatic potential that may result in PID and other cases that affect fertility.

Public health awareness campaigns have sought to improve the levels of awareness of the population with regard to STD screening. Some evidence suggests that screening rates have been improved and STD prevalence among risk populations has been contained because of educational interventions.[13] A meta-analysis published in 2019 also focused in the same area and concluded that early treatment gave positive results in the management of the disease's mentioned complications by 40-60% reduction in PID and more than 30% decrease in infertility due to STDs. [14]

For women diagnosed with an STD, it is important that they complete the entire course of prescribed antibiotics, and those that do are usually advised to attend a review appointment in order to check that the infection has cleared. An intervention [Partner notification] falls within this realm, notification and management of the partners go a long way in preventing re infection's safety of the woman and subsequently fertility risks.[15]

Public Health Implications & Recommendations

There is enough evidence to indicate that sexually transmitted diseases (STDs) in particular have dire implications on the public health particularly among the female fertility. Pertaining to multi-resistant gonorrhea, there is one more challenge which is non-resilient strains of STDs and its rising trend could undermine major global health strategies meant to control STDs by the year 2030. [10,11] As per a new report released by WHO, globally there are over 1 million infections per day that are easily curable and caused by STDs such as syphilis, gonorrhea, chlamydia, and trichomoniasis — a large number of them harm women's reproductive organs.[10] The issue of congenital syphilis and the loss of newborns at an early age is worsening, as the health care system was paralyzed by the coronavirus outbreak.[11]

In the United States of America, a new study from 2023 showed that in comparison with men, women have a larger health decrease owing to STDs infections. In comparison with men, the health quality-adjusted life years (QALYs) lost to infections, such as Chlamydia, are on the order of magnitude about 100 for women, which puts into perspective what this means for reproductive health and quality of life.[12,13] Late assessment followed by inertia when it comes to antibiotic treatment of sexually transmitted diseases cause additional damage all over the world: inability to conceive, ectopic pregnancy and periodic pain in the pelvic region. Of note is that these problems are frequently associated with patients that have limited economic means.[15,16]

Recommendations

Enhanced Screening and Surveillance: Increased routine screening for asymptomatic infections in sexually active populations is crucial. Programs should prioritize high-risk groups, including adolescents and pregnant women, to prevent complications like infertility and congenital STDs. (13,16)

Educational Campaigns: Community-based awareness initiatives on safe sexual practices,

early symptoms, and timely healthcare seeking are critical. Tailored messaging for adolescents and young adults can improve prevention efforts.[12,16]

Global Collaboration on Drug Resistance: Countries must adopt WHO's updated treatment guidelines to address rising antimicrobial resistance. Investments in research and development of novel antibiotics and vaccines are essential.[10,11]

Policy and Infrastructure Support: Governments should integrate STD prevention with broader reproductive health services. This includes subsidized testing, increased funding for reproductive health programs, and expanding access to fertility-preserving treatments for affected individuals.[10,16]

By adopting these measures, healthcare systems can mitigate the impacts of STDs on female fertility and align efforts with global targets to reduce disease burden and improve reproductive health outcomes.

Conclusion

The impact of STDs on female fertility is profound, with conditions like chlamydia and gonorrhea leading to complications such as PID and tubal damage that increase infertility and ectopic pregnancy risks. HPV-related cervical changes and interventions can further impact reproductive health, underscoring the multifaceted impact of STDs. The evidence highlights the critical need for preventive measures, regular screening, and prompt treatment to mitigate these effects and safeguard women's reproductive health.

To reduce the burden of STD-associated infertility, healthcare providers and policymakers must prioritize public health strategies that promote awareness, accessibility, and prevention. By addressing these needs, we can improve reproductive outcomes and protect the fertility of women globally.

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Viral Infections and their Fertility Options

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Viral infections are a threat to couples planning for pregnancy. The sexually transmitted nature of the viruses, such as HIV, HBsAg , and HCV, raises concern about transmission of the virus to their partner or their offspring. There is also a concern regarding the general health of the individual due to the nature of the infection, which can be chronic.

Therefore, adequate measures should be taken to improve the overall health of the individual and to prevent transmission to the offspring and partner. There has to be in-depth counseling for both the partners about the fertility options available and their implications. It depends on whether the male partner or the female partner is infected. The concerns with the female being infected are the vertical transmission and transmission to the male partner. The concern of a male being infected is transmission to the female partner.

Different types of viral infections and their fertility options:

The most common types of viral infections are HIV, HBSAG, HCV, and HPV. The less common are HTLV and Zika. The most common fertility options available are trying naturally with timed intercourse, IUI, ICSI or IVF based on the cause of infertility.

HBV virus

Hepatitis B virus (HBV) is one of the major viruses threatening global public health in humans, causing hepatic inflammation, cirrhosis, and hepatocellular carcinoma in patients. HBV is a disease that is transmitted through fluids; many studies also showed that HBV DNA can be detected in urine, saliva, and other tissues beyond the liver and blood.[1] HBV is not only able to pass through the blood-testis barrier and enter the sperm cell but also integrate into their sperm chromosome. As early as 1985, Hadchouel et al.[2] noticed the presence of HBV DNA in seminal fluid from HBV patients, suggesting the possibility of vertical transmission of HBV to the offspring.

1. **Prevention of transmission to the partner and offspring:** The non-infected partner should be vaccinated, and barrier methods of contraception should be used till the vaccination protocol is completed. The newborn should be vaccinated and given immunoglobulin prophylaxis at birth.[3]
2. **Assisted reproduction techniques and impact on outcomes:** The cause of infertility should decide the need for IUI, ICSI, or IVF. HBV virus can be found on eggs, sperm, or embryos; hence, there is a theoretical risk that remains to be proven. The couple should be counseled that the risk for vertical transmission remains even with MAR in females testing positive for HBV. There is no difference in MAR outcomes in males testing positive for HBV. Men with HBV infection will affect their sperm quality but not affect the outcomes of ART.[3]
3. **Prevention of transmission during MAR:** HBV DNA testing on semen samples is not recommended.There is no semen preparation available that can select HBV DNA-free sperm for MAR. Routine semen processing as per ESHRE guidelines on good practice in IVF laboratories should be done. (3)

HCV VIRUS:

Prevention of transmission to the partner and offspring: The most common mode of transmission of HCV is parenteral .It is also transmitted sexually. If a couple is in a monogamous relationship for more than a year, there is no need for barrier methods. There is no vaccination available for HCV infection. However, antiviral treatments are available. It is recommended that patients complete the course of antiviral treatment for HCV before starting MAR, as antivirals used for HCV infection are contraindicated in pregnancy.(4) The risk of vertical transmission cannot be nullified if a female is HCV positive. Caesarean delivery is not recommended based on HCV positivity. Breastfeeding is also not contraindicated.[3]

Assisted reproduction techniques and impact on outcomes: The cause of infertility decides the need for IUI/IVF/ICSI. MAR does not eliminate the risk of vertical transmission in cases where the female is HCV positive. The possibility of HCV viral RNA presence in oocytes cannot be excluded. However, the risk of HCV transmission through the use of reproductive material remains to be proven. There are contradictory results evaluating the effects of male and female HCV infection on infertility treatment outcomes. Although the fertilization rate has been reported to be significantly lower in couples with HCV-RNA-positive men, other studies report that HCV infection does not affect the IVF-ICSI cycle outcomes in these couples. Although some studies report significantly reduced implantation rates, higher cycle cancellations, and higher FSH use in HCV-positive women, others report no significant differences.[3]

Semen Processing:

The semen preparation method recommended for HCV-positive men is a discontinuous double density gradient followed by swim up and wash. Current evidence shows that semen can test positive for HCV after single continuous density centrifugation or after discontinuous density centrifugation without wash steps. After advanced semen processing, PCR testing for HCV is not necessary. Good laboratory practice regarding semen processing should be applied irrespective of whether only the male or both partners are testing positive for HCV.(3)

HPV:

The human papillomavirus (HPV) is a non-enveloped, double-stranded, circular DNA virus that is responsible for causing multiple epithelial lesions and cancers. It can manifest as cutaneous and anogenital warts, which, depending on the subtype, may progress to carcinoma. It can infect both men and women. It usually clears off from the body within 1-2 years. If it persists, it can lead to genital warts and cancer.[6]

Prevention of transmission to the partner and offspring

Barrier methods of contraception are advisable to prevent HPV infection in the partner. It is recommended to evaluate for HPV-related lesions in females before MAR. There is no evidence that there is a specific HPV DNA copy number threshold below which horizontal or vertical transmission is unlikely.

Assisted reproduction techniques and impact on outcomes:

The cause of infertility should dictate the specific technique (IUI/IVF/ICSI) used for MAR in couples where one or both partners test positive for HPV. MAR does not eliminate the risk of vertical transmission. The possibility of HPV testing could be discussed with couples undergoing IUI. Couples with a known positive HPV test should be advised that HPV is a transient infection, and postponing MAR treatment is an option depending on the individual circumstances.[3]

Prevention/reduction of transmission during assisted reproduction

There is weak evidence that therapeutic HPV vaccination in HPV-positive men may increase pregnancy rates in natural conception and reduce miscarriage rates. No current semen preparation technique can eliminate the virus from the infected semen sample.[3]
Reducing or avoiding vertical transmission
A caserean section is not recommended on the basis of HPV positivity alone. Breastfeeding is not contraindicated.[3]

HTLV 1 & 2

Prevention of transmission before medically assisted reproduction

There is a risk of sexual transmission of the virus to the unaffected partner. To reduce this risk, couples could be advised to use barrier contraception and receive reproductive counseling if they want to conceive. Based on current evidence, we cannot define a threshold of HTLV I/II viral load below which horizontal or vertical transmission of HTLV I/II is not occurring.[3]

Assisted reproduction techniques and impact on outcomes

There is strong evidence that the cause of infertility should dictate the specific technique (IUI/IVF/ICSI) used for medically assisted reproduction (MAR) in couples where one or both partners test positive for HTLV I/II. From the perspective of horizontal and vertical transmission, there is currently not enough evidence to recommend one technique (IUI/IVF/ICSI) over another in patients infected with HTLV I/II. MAR does not eliminate the risk of vertical transmission. The possibility of HTLV I/II presence in gametes or placenta cannot be

confirmed or excluded. To date, the risk of HTLV I/II transmission through the use of infected semen or oocytes remains to be proven. The impact of female HTLV I infection on MAR outcomes remains unknown.[3]

Prevention/reduction of transmission during assisted reproduction

There are no techniques known for prevention/reduction of transmission of HTLV I/II during MAR.[3]

Reducing/avoiding vertical transmission

Caesarean delivery is not recommended on the basis of maternal HTLV I/II positivity alone. There is only very limited and low-quality evidence comparing the risk of vertical transmission between vaginal and caesarean delivery. A female testing positive for HTLV I/II should refrain from breastfeeding when and where she has safe nutritional alternatives.[3]

Zika virus

Prevention of transmission before medically assisted reproduction

A male diagnosed with ZIKV infection or returning from a ZIKV endemic region should use barrier contraception with any partner for 3 months. A female diagnosed with ZIKV infection or returning from a ZIKV-endemic region should use barrier contraception and avoid pregnancy for 2 months. There is no agreed threshold described in the literature below which transmission is unlikely. We advocate the use of barrier contraception to prevent horizontal transmission and avoiding pregnancy for 3 months after diagnosis or return from a ZIKV endemic area to reduce vertical transmission.[3]

Assisted reproduction techniques and impact on outcomes

If a patient or partner has been diagnosed with ZIKV infection or returned from a ZIKV endemic region in the last 3 months, medically assisted reproduction (MAR) treatment should be postponed. In the case of fertility preservation, the approach should be tailored to the individual situation. In the case of fertility preservation, there is insufficient data on the risk of viral transmission using gametes potentially infected with ZIKV. An individual risk assessment is advised before using these gametes. There is insufficient evidence on the association between Zika infection and gametes or the potential of transmission to offspring in the absence of maternal infection. If ZIKV-infection is diagnosed in male or female during MAR treatment, the cycle should be stopped, and the couple should be advised to use barrier contraception for 3 months.[3]

Prevention/reduction of transmission during assisted reproduction

There are currently no semen processing techniques available that can completely remove ZIKV from semen. MAR is not advised even if male serum is free of ZIKV because of the poor correlation between serum and semen viral load. All infected patients, regardless of viral load, may be infectious through semen. The clearance of Zika virus is slower from semen compared to blood. Therefore, a negative test in plasma or serum does not offer 100% reassurance.[3]

Reducing/avoiding vertical transmission

ZIKV has been found in the breast milk of women with confirmed ZIKV infection. The possibility of transmission of ZIKV through breastfeeding has only been assessed in 12 mother-child pairs. This provides insufficient evidence to establish a recommendation. (3)

	TYPE OF INFECTION	VACCINE AVAILABLE	Horizontal/Vertical Transmission	HORIZONTAL TRANSMISSION DURING MAR	PRVENTION OF VERTICAL TRANSMISSION BY CS	VERTICAL TRANSMISSION VIA BREASTFEEDING	PROPHYLAXIS IN NEONATE
HBV	ACUTE / PERSISTENT	YES	YES	YES- VACCINATE AFFECTED PPARTNER	PROBABLY NOT	PROBABLY NOT	YES
HCV	ACUTE / PERSISTENT	NO	LIMITED	LIMITED	PROBABLY NOT	PROBABLY NOT	NO
HPV	TRANSIENT	YES	YES	YES	PROBABLY NOT	PROBABLY NOT	NO
HTLV1 /2	ACUTE / PERSISTENT	NO	YES	YES	UNKNOWN	YES	NO
ZIKA	TRANSIENT	NO	YES	YES	PROBABLY NOT	UNKNOWN	NO

Figure 1: Summary

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Emerging Trends in ART

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Since its inception in 1978, the field of assisted reproduction has seen rapid advancements.
Initially developed to help the infertile couple, we have seen rapid expansion in clinical indications for IVF including medical, genetic conditions as well as fertility preservation over the past few decades.[1] Many of the advances in ART have both improved chances of success rates and offered a large range of options of treatment to couples.[2] This article explores some of the most significant cutting edge innovations in assisted reproduction, including innovations in technology, medical advancements and scientific advancements.

1. Medical Advancements

Controlled ovarian hyperstimulation (COH) is done to increase the number of oocytes for IVF. It involves multiple injections of gonadotropins and continuous visits to the clinic for transvaginal ultrasounds and monitoring of circulating hormone levels. Nowadays utilization of long-acting gonadotropins like corfollitropin-alpha, corfollitropin-delta which has to be given once weekly or oral medications like oral antagonist elagolix are available and studies are going on worldwide for its acceptance.[3,4] Similarly, a new strategy to measure salivary estradiol levels may help reduce the need for blood samplings during COH.[5] Recent advancements in radiological field in the form of portable lower cost ultrasound devices and self-operated endovaginal telemonitoring may further ease the follicular and endometrial monitoring.[6]

1. Technological advancements in laboratories

The initial steps in the IVF laboratory are finding and separating sperm and oocytes, fertilization, embryo culture, selecting embryo for transfer and freezing of excess embryos and gametes. Large progress has been made for automation of these individual steps by way of novel technologies.[7]

a. Microfluidics: It is a new IVF lab-on-a-chip concept in which automation of nearly all necessary steps are there in a single system. Microfluidics technology controls fluids of microliters to picoliters within a network of channels with size from tens to hundreds of micrometers. Microfluidics offers unique advantages, like reduced reagent volume, short reaction time, and the scalability for parallel operation, allowing Miniaturization and automation. Microfluidics offers an alternative to almost every step in the process of IVF, like enhanced selection of motile sperm even from testicular biopsies, automated processing of oocytes, in vitro follicle growth, embryo culture, and cryopreservation. Furthermore, the ability to reproduce a given single IVF procedure on an isolated microfluidic device offers the chance to investigate and understand the reproductive physiology in each step of assisted human reproduction.Potentially, intracytoplasmic sperm injection (ICSI) will not be necessary in the future thanks to lab on chip devices.[8]

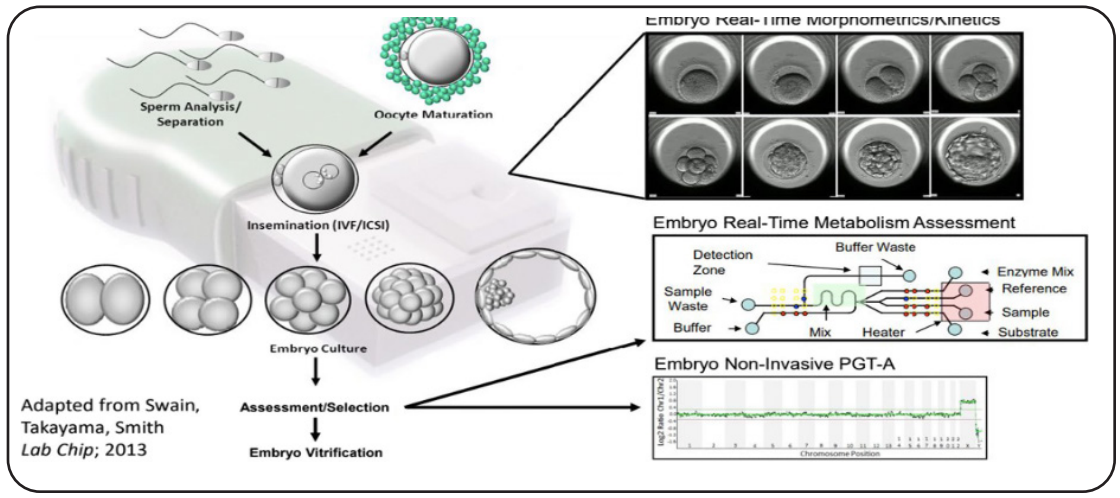


Figure 1: Future IVF lab-on-a-chip concept showing the integration of all the steps of IVF and of emerging non-invasive techniques of embryo assessment[1]

b. Preimplantation Genetic Testing (PGT) invasive and non invasive: One of the most notable developments in IVF is the development of Preimplantation Genetic Testing (PGT). PGT helps in the screening of embryos for genetic abnormalities before implantation. Although the purpose of PGT-A was to increase implantation rates, decrease time to pregnancy and improve live birth rates , but RCT and other studies have been inconclusive.

Figure 1: Future IVF lab-on-a-chip concept showing the integration of all the steps of IVF and of emerging non-invasive techniques of embryo assessment[1]

Minimally invasive PGT is done by aspirating blastocoel fluid with an ICSI needle. The fluid includes embryonic cells and cfDNA.NGS or PCR is done on fluid to detect any chromosomal abnormalities. Similarly, Noninvasive PGT involves testing the spent culture media in which embryo were cultured. Molecules such as cfDNA, RNA, and metabolites are released into the culture media as the cells grow which is examined by NGS, PCR, or microarray analysis. These techniques are less invasive, less damage to the fetus, less chances of mosaicism, improved efficacy and accuracy but are costly, have high false positive and negatives and technological constraints.[9]

c. Time-Lapse Imaging: Time Lapse Imaging is another breakthrough in noninvasive evaluation of developing embryos. Early embryogenesis is a dynamic process, which can be monitored using incubators equipped with built in time lapse and video equipment that allow the real time evaluation of these dynamic changes which can help embryologist select embryos best suited for uterine transfer in IVF cycles without the need for removing the dishes from incubators. Although, the evidence regarding its use is inconclusive.[10]

d. OMICS: Although advances in ART, such as new strategies for oocyte stimulation, oocyte/embryo freezing or the transfer of chromosomally healthy embryos, have increased pregnancy rates, no technique can yet predict or control the embryo's capability to attach to the maternal endometrium. A better understanding of the physiological and molecular factors involved in this process is crucial for designing effective strategies to improve pregnancy rates. Study of such factors is known as OMICS which includes genomics, transcriptomics, proteiomics, metabolomics, exomics (analysis of exons), epigenomics (assessment of epigenetic modifications), secretomics (analysis of secreted products) and lipidomics (large-scale analysis of the whole lipid species. ERA which is endometrial receptivity array is a transcriptomic study of 238 genes expressed in a receptive endometrium has been in use to assess window of implantation suitable for embryo transfer especially in recurrent implantation failure although studies are inconclusive for its use currently.[11]

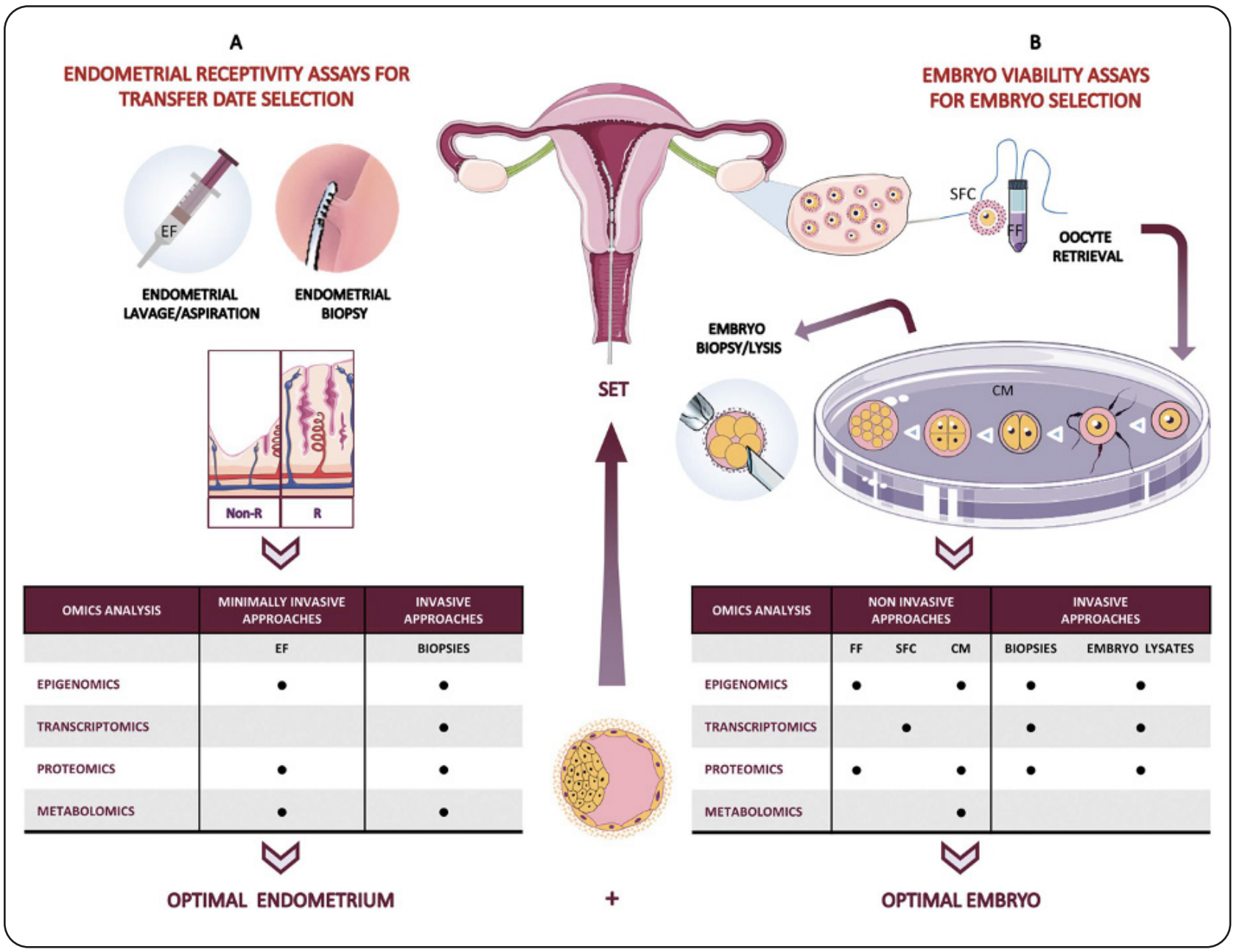


Figure 3: Multiomics model[11]

e. Artificial Intelligence (AI) and Machine Learning: The collaboration of AI and machine learning into IVF processes is gaining momentum. AI includes machine learning (ML), robotics, and computer vision.12 These technologies aims to increase the precision and efficiency of IVF procedures. AI-based algorithms are being used for semen analysis of various parameters like motility, morphology and DNA integrity. The purpose of Computer-aided sperm analyzers (CASA) is to reduce intra-operator subjectivity and variability linked with manual assessment thereby aiding in the selection of best sperm. It has also shown good correlation with manual assessment. Nowadays portable smart phone-based CASA devices are also available.13 Since the use of AI has come, it has increased success of microsurgical testicular sperm extraction (micro-TESE) procedures. AI is also being experimented for uses in pre-treatment counselling, oocyte assessment, dosage of gonadotropin administration, triggering of oocytes for maturation, embryo assessment for ploidy selecting best embryo for transfer. Further prospective studies needed including heterogenous population for conclusive evidence of benefits.[14]

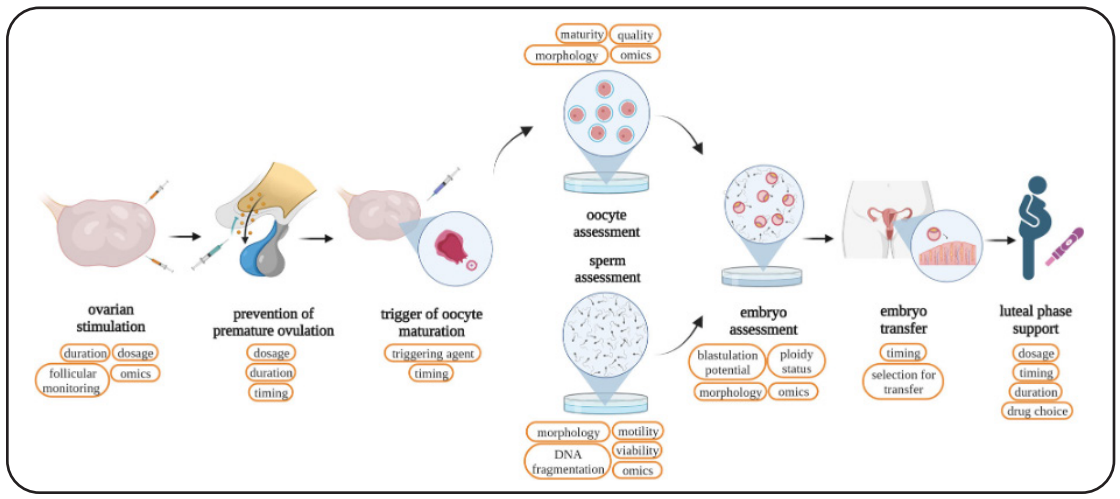


Figure 4: Potential targets of artificial intelligence in assisted reproductive technology[14]

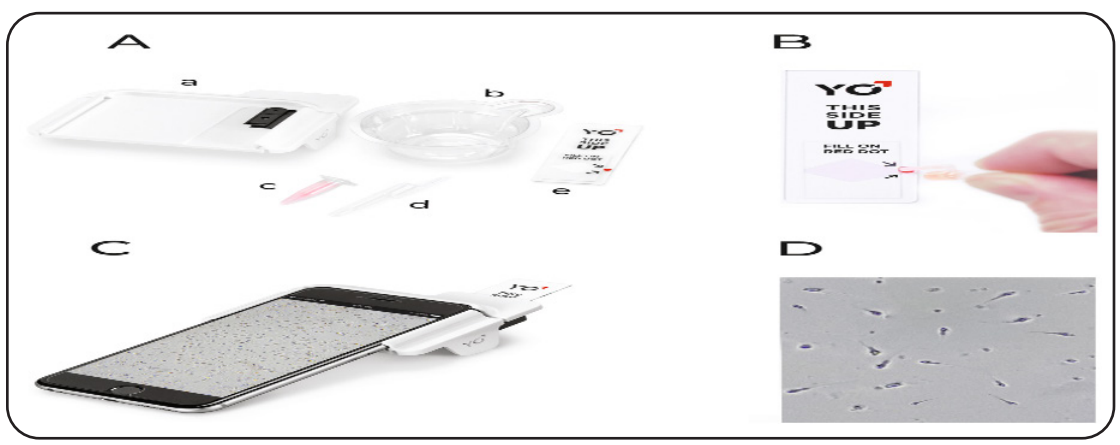
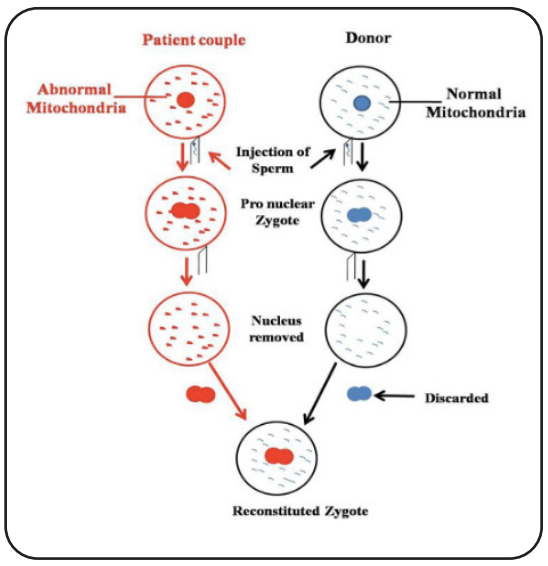


Figure 5: Smart phone based CASA semen analyser[13]

2. Scientific advancements

a. CRISPR-Cas9 Technology: CRISPR-Cas9, a biotechnological advancement, which allows for precise modifications of the genome, offering the possibility of correcting genetic defects at the embryonic stage. While still largely experimental, CRISPR-Cas9 has been experimented for correction of mutations for preventing monogenic genetic disorders and improving the phenotype of offspring.[7,12]

b. Mitochondrial Replacement Therapy (MRT): Mitochondrial replacement therapy (MRT) is a evolving technique in invitro fertilization (IVF) which involves replacing a women's abnormal mitochondrial DNA (mt-DNA) with the donor's healthy mtDNA to prevent transmission of mitochondrial diseases from mother to child. MRT involves various techniques like spindles transfer (ST), pronuclear transfer (PNT) or polar body transfer (PBT). In aged individuals, this technique has also been explored through in vitro fertilization, by substituting defective cytoplasm of aged mother with healthy one from donor to enhance the chances of pregnancy rate. However, there are moral, social, and cultural objections which have restricted its use also there are risk of heteroplasmy and no offspring due to mito-nuclear incompatibility.[15]



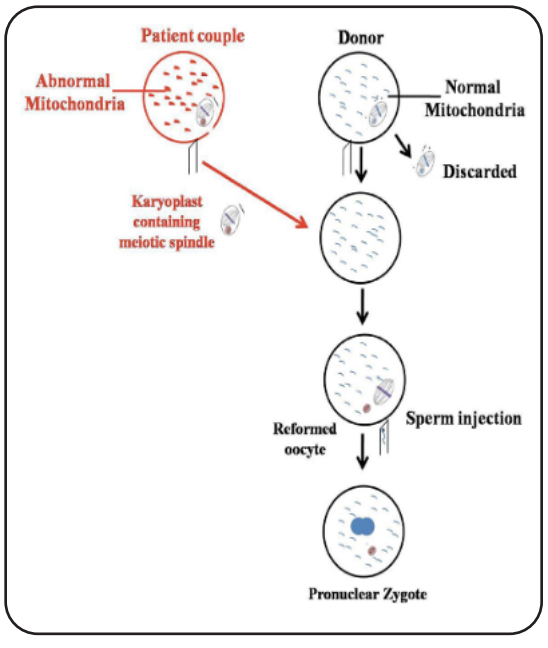


Figure 6- Techniques of mitochondrial transfer[15]

c. Stem Cell therapy: Stem cell therapy is a promising therapy explored for the treatment of ovarian dysfunction, particularly in cases of premature ovarian insufficiency (POI). Characterized by the loss of ovarian function before the age of 40, POI poses difficulty for women to conceive, often leading to infertility. Stem cells are categorized into pluripotent and multipotent categories according to their potential for differentiation. Pluripotent stem cells--such as embryonic stem cells (ESCs)-are the ones which can covert into tissues derived from all three germ layers. Conversely, induced pluripotent stem cells (iPSCs) and mesenchymal stem cells (MSCs) are other sources of pluripotent and multipotent stem cells, respectively: iPSCs are derived through cellular reprogramming, whereas MSCs are retrieved from adult tissues such as bone marrow, fat or umbilical cord. The therapeutic potential of stem cells has been explored extensively in POF in animal studies. But it is difficult to extrapolate results from animal studies to human model, although a lot of human studies are underway there are ethical concerns of cloning as well as chances of epigenetic changes in the gametes formed.[12,16]

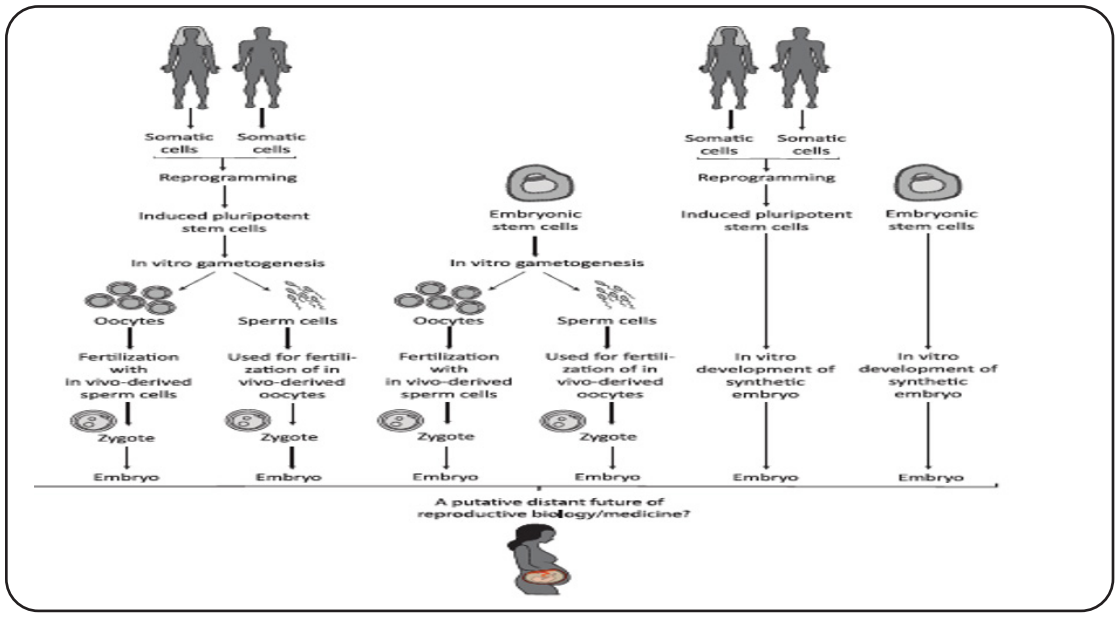


Figure 7: Schematic representation of stem cell therapy[16]

d. Ovarian rejuvenation:

Ovarian PRP: is one technique that uses platelet-rich plasma retrieved from a woman's blood to increase ovarian function and fertility outcomes. It enhances the growth and maturation of healthy eggs and help in conditions such as diminished ovarian reserve and primary ovarian insufficiency by increasing the number of eggs retrieved.[12]

Artificial ovaries and in vitro activation: Young women who are undergoing cancer treatment or suffering from POF can help conceive a child through these new techniques which involves usage of hydrogels and scaffolds in which isolated follicle from ovarian tissue is transplanted to create microenvironments required for ovarian cell growth and function or by disrupting Hippo signalling and Akt stimulation of cortical strips can reactivate follicular growth in vivo. Conventional fertility preservation methods such as oocyte or embryo cryopreservation are currently not sufficient to treat patients with prepubertal cancer and premature ovarian failure. Although, Ovarian tissue cryopreservation is an alternative but has a potential risk of reintroducing malignant cells in patients who suffered from cancer. So this technique can be of use in these patients as in trials done on humans it can restore endocrine function, achieve in vivo follicular growth and has also achieved pregnancies. However it is still largely experimental due to safety concerns or ethical concerns of genetic modification.[12]

e. Advancements for uterine problems:

Uterine Transplant: Recent advancements in surgical techniques and immunosuppressive therapies have enhanced the success rates of uterine transplants, facilitating women without a functional uterus to experience pregnancy and childbirth.

Artificial womb: An artificial womb is a device or system which replicate natural womb for the development of a fetus outside the human body. As of now it is still experimental , studies have been conducted on lambs which have grown up to 28 weeks, but developing till term is still experimental and human trials are yet to take place. The main purpose of this technology is to improve outcomes for premature infants, offering alternatives for those with fertility issues, and potentially advancing research in fetal development.[17]

Conclusion

The field of assisted reproduction is undergoing remarkable innovation and transformation. Advances in technology at each level are shaping the future of fertility treatments. As these emerging trends continue to evolve, they hold promising results for infertile couples in future to improve their outcomes, while also addressing complex ethical and societal issues. The continued progress in this field promises to offer new opportunities and solutions for those facing reproductive challenges, ultimately contributing to the broader understanding of human fertility and family building.

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Calender of Events

All IFS Activities 2024-26

Over 260 Programs/CMEs/Meetings Conducted

Activity Date	Activity Day	Chapter/SIG / Zone / Joint/ Other	Activity Name	Mode	Time
01.08.2024	Thursday	SIG + Chapter	SIG: PCOS with UP East Chapter	Online Webinar	4.00 pm - 7.00 pm
02.08.2024	Friday	SIG	SIG: Counselling & Patient Support with ASRM Academy	Online Webinar	6.00 pm - 7.00 pm
02.08.2024	Friday	SIG + Chapter	SIG: Early Pregnancy & With Chandigarh Chapter	Online Webinar	6.00 pm - 7.00 pm
05.08.2024	Monday	2 SIG + Chapter	SIG: Endometrosis & Endoscopy with North East Chapter	Online Webinar	4.00 pm - 5.30 pm
06.08.2024	Tuesday	SIG	SIG: Reaserch Methodology	Online Webinar	5.30 pm - 8.30 pm
07.08.2025	Wednesday	Chapter	IFS MP - Chapter Activity (Polaris)	Online Webinar	5.00 pm - 7.00 pm
07.08.2025	Wednesday	SIG + Chapter	SIG: KIP with Vidarbha Chapter	Online Webinar	6.30 pm - 8.30 pm
08.08.2024	Thursday	SIG + Chapter	SIG: Embryology with Tamilnadu chapter	Online Webinar	5.30 pm - 7.30 pm
08.08.2024	Thursday	2 SIG	SIG: Environment & Infertility with Holistic Medicine	Online Webinar	6.00 pm - 8.00 pm
09.08.2024	Friday	Pharma CME - Gurugram	IFS Haryana chapter with Nationa Series of Physical CME - InterMedics	Physical	11.00 pm - 2.00 pm
09.08.2024	Friday	Central - YEP	IFS - Young Turks Journal Club - Activity	Online Webinar	7.00 pm - 8.00 pm
10.08.2024	Saturday	SIG	SIG: Fertility Preservation	Physical	12.00 pm - 3.00 pm
11.08.2024	Sunday	Pharma CME - MP	IFS MP chapter with Nationa Series of Physical CME - Celeganix Pharma	Physical	11.00 am - 02.00 pm
11.08.2024	Sunday	Pharma CME - Chhattisgarh	IFS Chhattisgarh chapter with Nationa Series of Physical CME - Sun Pharma	Physical	11.00 pm - 2.00 pm
11.08.2024	Sunday	Central - NEP	Nursing - Empowerment Program (Nightangle)	Online Webinar	7.00 pm - 8.00 pm
11.08.2024	Sunday	Chapter	IFS Odisha - Installation Ceremony (Dr Pankaj Sir & Dr Niti Vijay Ma'am)	Physical	10.00 am - 4.00 pm
11.08.2024	Sunday	Chapter	UP East - Chapter Quiz	Online Webinar	11.00 am - 12.00 pm
12.08.2024	Monday	Chapter	IFS Uttrakhand - Chapter Activity	Online Webinar	4.30 pm - 6.30 pm
12.08.2024	Monday	Central - CEP	IFS - Counsellor Empowerment Program	Online Webinar	6.00 pm - 7.00 pm
13.08.2024	Tuesday	SIG	SIG: Reproductive Endocrinology	Online Webinar	6:30 pm - 8:00 pm
14.08.2025	Wednesday	Chapter	IFS MP - Chapter Activity (Masterclasses)	Online Webinar	6.00 pm - 8.00 pm
14.08.2025	Wednesday	Central - iEP	AI Naturally - AI in ART	Online Webinar	6.00 pm - 7.00 pm
16.08.2024	Friday	SIG + Chapter	SIG: Endoscopy with IFS MP Chapter (Sudeeksha 2.0)	Online Webinar	9.00 am - 1.00 pm
17.08.2024	Saturday	2 SIG + Chapter	SIG: Counselling & Holistic Medicine IFS MP - Chapter Activity (Sahyog)	Online Webinar	5.00 pm - 7.00 pm
18.08.2024	Sunday	Central - EBM	IFS Mid Term Meet + Executive Body Meet (EBM) (India Habitat Centre)	Physical	9.00 am - 5.00 pm
20.08.2024	Tuesday	Central - SEP	IFS - Self Empowerment Program	Online Webinar	5:00 pm - 6:00 pm
21.08.2024	Wednesday	Chapter	IFS Odisha - Chapter Activity	Online Webinar	Half Day
22.08.2024	Thursday	Chapter	IFS Pondicherry - Chapter Activity	Physical	6:00 pm - 8:00 pm
23.08.2025	Friday	2 SIG + Chapter	SIG: Ultrasound & Endoscopy with South Tamilnadu Chapter	Physical	6:00 pm - 8:00 pm
23.08.2024	Friday	Chapter	IFS Uttrakhand - Installation Ceremony (Dr Pankaj Sir & Dr Shalini Chawla Khanna Ma'am)	Physical	6:00 pm - 9:00 pm
24.08.2024	Saturday	Chapter	Bihar Chapter - 2nd Annual Conference (Day 1) (Dr Pankaj Sir & Dr Shweta Mittal Ma'am)	Physical	Full Day
25.08.2024	Sunday	Chapter	Bihar Chapter - 2nd Annual Conference (Day 2)	Physical	Full Day
28.08.2024	Wednesday	SIG	SIG: QA & QC in ART	Online Webinar	5.30 pm - 7.30 pm

Activity Date	Activity Day	Chapter/SIG / Zone / Joint/ Other	Activity Name	Mode	Time
28.08.2025	Wednesday	SIG	SIG: POR	Online Webinar	6.00 pm - 8.00 pm
28.08.2025	Wednesday	Central - PEP Phase 2	Launching of PEP Phase - 2 in 6 states	Physical	12.00 pm - 2.00 pm
29.08.2024	Thursday	Central Trade Meet	Trade Meeting in Delhi - Hotel Pride Plaza (Dr Pankaj & Dr Shweta Mittal)	Physical	7.00 pm - 10.00 pm
29.08.2024	Thursday	SIG + Chapter	SIG: Genital Tuberculosis with MP Chapter Activity	Online Webinar	7.00 pm - 8.00 pm
30.08.2025	Friday	Chapter Quiz	IFS Haryana - Chapter Quiz Kahoot	Online Webinar	4.00 pm - 5.00 pm
30.08.2025	Friday	Chapter	IFS MP Chapter - Master Classes Activity	Online Webinar	7.00 pm - 8.30 pm
30.08.2025	Friday	Central - YEP	IFS - Young Turks Journal Club - Activity	Online Webinar	7.00 pm - 8.00 pm
30.08.2025	Friday	Central - Quiz	IFS Quiz - Genius Junction Monthly Quiz	Online Webinar	7.30 pm - 8.00 pm
31.08.2024	Saturday	Chapter Quiz	IFS Haryana Chapter Activity	Physical	2.00 pm - 5.00 pm
31.08.2024	Saturday	Chapter	IFS Karnataka - Installation Ceremony (Dr Pankaj Sir & Dr Rashmi Sharma)	Physical	6.00 pm - 9.00 pm
01.09.2024	Sunday	Chapter	IFS Telangana - Installation Ceremony (Dr Pankaj Sir & Dr Renu Tanwar)	Physical	11.00 am - 2.00 pm
01.09.2024	Sunday	Chapter Quiz	IFS MP - Chapter Quiz on Kahoot	Online Webinar	12.00 pm - 12.45 pm
04.09.2024	Wednesday	2 Chapters	IFS MP & North East - Sukanya Activity (PCOS Aweness)	Physical	
04.09.2024	Wednesday	Chapter	IFS MP - Chapter Activity (Polaris)	Online Webinar	4.00 pm - 7.00 pm
06.09.2024	Friday	SIG + Chapter	SIG: Endoscopy with MP Chapter (Sudeeksha 2.0)	Physical	09.00 am - 01.00 pm
08.09.2024	Sunday	Pharma CME - Bareilly	IFS UP West chapter with Nationa Series of Physical CME - Sun Pharma	Physical	1.00 pm - 5.00 pm
08.09.2024	Sunday	Central - NEP	IFS - Nursing Empowerment Program (Nightangle)	Online Webinar	7.00 pm - 8.00 pm
08.09.2024	Sunday	Chapter Quiz	IFS Vidarbha - Chapter Quiz on Kahoot		
10.09.2024	Tuesday	Chapter	IFS MP - Sukanya PCOS Awareness Activity	Physical	10.00 am - 12.00 pm
10.09.2024	Tuesday	SIG + Chapter	SIG: Endrometrosis with MP Chapter (Sudeeksha 2.0)	Physical	09.00 am - 01.00 pm
12.09.2024	Thursday	SIG	SIG: Genital Tuberculosis with MP Chapter Activity	Online Webinar	7.00 pm - 8.00 pm
13.09.2024	Friday	Central - YEP	IFS - Young Turks Journal Club - Activity	Online Webinar	7.00 pm - 8.00 pm
13.09.2024	Friday	Fusion	Fusion 2024 at Jaipur (Day 1)	Physical	Full Day
14.09.2024	Saturday	Fusion	Fusion 2024 at Jaipur (Day 2)	Physical	Full Day
15.09.2024	Sunday	Fusion	Fusion 2024 at Jaipur (Day 3)	Physical	Full Day
19.09.2024	Thursday	3 Chapters	IFS MP, Punjab & North East - Chapter Activity (Bharat Sangam)	Online Webinar	6.00 pm - 8.00 pm
19.09.2024	Thursday	Chapter	IFS Vidarbha - Chapter Activity	Online Webinar	6.00 pm - 9.00 pm
20.09.2024	Friday	Central - EBM	Monthly Meet - Executive Body Meet (EBM)	Physical	5.00 pm - 7.00 pm
21.09.2024	Saturday	Pharma CME - Shivani	IFS Rajasthan chapter with Nationa Series of Physical CME - Shivani Pharma	Physical	6.00 pm - 9.00 pm
22.09.2024	Sunday	Chapter	IFS MP - Installation Ceremony (Dr Pankaj Sir & Dr Shweta Ma'am)	Physical	11.00 am - 2.00 pm
22.09.2025	Sunday	Chapter	IFS West Bengal - IUI Workshop at Kota	Physical	10.00 am - 2.00 pm
23.09.2024	Monday	Chapter	IFS West Bengal - Activity Health Awareness Camp	Physical	3.00 pm - 5.00 pm
24.09.2024	Tuesday	Central - CEP	Counsellor Empowerment Program	Online Webinar	6.30 pm - 7.30 pm
24.09.2024	Tuesday	Central - SEP	Self Empowerment Program	Online Webinar	5.00 pm - 6.00 pm
26.09.2024	Thursday	SIG + Chapter	SIG: PCOS with Chhattisgarh Chapter Activity	Online Webinar	4:00pm-5:30pm
26.09.2024	Thursday	SIG	SIG: Genital Tuberculosis with MP Chapter Activity	Online Webinar	7.00 pm - 8.00 pm

Activity Date	Activity Day	Chapter/SIG / Zone / Joint/ Other	Activity Name	Mode	Time
27.09.2024	Friday	Central - YEP	IFS - Young Turks Journal Club - Activity	Online Webinar	8.00 pm - 9.00 pm
27.09.2024	Friday	Central - Quiz	IFS Quiz - Genius Junction Monthly Quiz	Online Webinar	7.30 pm - 8.00 pm
28.09.2024	Saturday	Chapter Quiz	IFS Chhatisgarh - Chapter Quiz on Kahoot	Online Webinar	5.00 pm - 6.00 pm
29.09.2024	Sunday	Chapter Quiz	IFS UP East - Chapter Quiz on Kahoot	Online Webinar	4:30 pm-5:30 pm
29.09.2024	Sunday	Pharma CME - Lucknow	IFS UP East - Chapter Activity InterMedics	Physical	1.00 pm - 5.00 pm
01.10.2024	Wednesday	SIG	SIG: Endrometrosis	Online Webinar	4.00 pm - 6.00 pm
02.10.2024	Thursday	Chapter	IFS MP Chapter Activity (Polaris)	Online Webinar	5.00 pm - 7.00 pm
04.10.2024	Friday	SIG	SIG Reproductive Endocrinology	Online Webinar	3.30 pm - 5.00 pm
04.10.2024	Friday	Chapter	IFS Haryana Chapter Activity with Karnal obs & gyn society	Online Webinar	7.00 pm - 9.00 pm
04.10.2024	Friday	Central - CEP	IFS - Counsellor Empowerment Program	Online Webinar	4.00 pm - 5.00 pm
06.10.2024	Sunday	Pharma CME - Sun	IFS Telangana chapter with Nationa Series of Physical CME - Sun Pharma	Online Webinar	11.00 am - 1.00 pm
06.10.2024	Sunday	SIG + Chapter	SIG: Genetics with IFS Karnataka Chapter CME	Physical	11.00 am - 3.00 pm
06.10.2024	Sunday	SIG + Chapter	SIG: Reproductive Endocrinology (Surat)	Physical	Full Day
08.10.2024	Tuesday	Central - CEP	Counsellor Empowerment Program	Online Webinar	6.00 pm - 7.00 pm
10.10.2024	Thursday	Chapter	IFS Chhattisgarh - One day Annual Conference	Physical	Full Day
10.10.2024	Thursday	SIG + Chapter	SIG: Genital Tuberculosis with MP Chapter Activity	Online Webinar	7.00 pm - 8.00 pm
11.10.2024	Friday	SIG	SIG: Reproductive Endocinology	Online Webinar	4.00 pm - 6.00 pm
11.10.2024	Friday	Central - YEP	IFS - Young Turks Journal Club - Activity	Online Webinar	7.00 pm - 8.00 pm
13.10.2024	Sunday	Central - NEP	IFS - Nursing Empowerment Program (Nightangle)	Online Webinar	7.00 pm - 8.00 pm
15.10.2024	Tuesday	Chapter	IFS Odisha Chapter Activity	Physical	6.30 pm - 9.30 pm
15.10.2024	Tuesday	Chapter Quiz	IFS Chhatisgarh - Chapter Quiz on Kahoot	Online Webinar	4.00 pm - 5.00 pm
16.10.2024	Wednesday	Chapter	IFS MP Chapter Suraksha Webinar	Online Webinar	5.00 pm - 7.00 pm
16.10.2024	Wednesday	Central - Delhi Foum	IFS Delhi Forum Meeting	Physical	1.00 pm - 5.00 pm
17.10.2024	Thursday	Zonal Quiz	IFS South Zone Quiz (Tamilnadu, Bengaluru, Odisha, Pondicherry, South TN)	Online Webinar	6.00 pm - 7.00 pm
18.10.2024	Friday	Chapter Quiz	IFS Andhra Pradesh - Chapter Quiz on Kahoot	Online Webinar	7.00 pm - 8.00 pm
18.10.2024	Friday	Chapter Quiz	IFS Karnataka - Chapter Quiz on Kahoot	Online Webinar	6.00 pm - 7.00 pm
18.10.2024	Friday	Central - EBM	Monthly Meet - Executive Body Meet (EBM)	Physical	5.00 pm - 7.00 pm
19.10.2024	Saturday	Pharma CME - Caleganix	IFS West Bengal chapter with Nationa Series of Physical CME - Celeganix Pharma	Physical	7.00 pm - 11.00 pm
19.10.2024	Saturday	Chapter Quiz	IFS Telangana & Andhra Chapter Quiz on Kahoot	Online Webinar	4.00 pm - 5.00 pm
20.10.2024	Sunday	Chapter Quiz	IFS South TN & Pondicherry Chapter Quiz on Kahoot	Online Webinar	11.00 am - 12.00 pm
20.10.2024	Sunday	Chapter	IFS Kerala Chapter Activity	Physical	9.00 am - 1.30 pm
21.10.2024	Monday	SIG	SIG: Research & Methodology	Online Webinar	4.00 pm - 5.30 pm
22.10.2024	Tuesday	SIG	SIG Endoscopy with Kota OBG Society	Online Webinar	4.00 pm - 6.00 pm
22.10.2024	Tuesday	Chapter Quiz	IFS Kerala - Chapter Quiz on Kahoot	Online Webinar	7.00 pm - 8.00 pm
24.10.2024	Thursday	SIG	SIG: Genetics with ACE Webinar CME	Online Webinar	6.30 pm - 8.00 pm
24.10.2024	Thursday	Chapter	IFS Vidarbha Chapter Activity	Physical	7.30 pm - 10.00 pm

Activity Date	Activity Day	Chapter/SIG / Zone / Joint/ Other	Activity Name	Mode	Time
25.10.2024	Friday	Chapter	IFS Haryana Chapter PCOS Awareness Activity	Physical	Half Day
25.10.2024	Friday	Central - YEP	IFS - Young Turks Journal Club - Activity	Online Webinar	8.00 pm - 9.00 pm
26.10.2024	Saturday	Central - Quiz	IFS Quiz - Genius Junction Monthly Quiz	Online Webinar	7.30 pm - 8.00 pm
26.10.2024	Saturday	Pharma CME - Shivani	IFS Tamilnadu chapter with Nationa Series of Physical CME - Shivani Pharma	Physical	6.00 pm - 9.00 pm
26.10.2024	Saturday	Chapter	IFS Haryana Chapter PCOS Awareness Activity	Physical	Half Day
26.10.2024	Saturday	SIG	SIG: PCOS Activity	Online Webinar	4.00 pm - 6.00 pm
27.10.2024	Sunday	Chapter Installation	IFS North East - Installation Ceremony (Dr Pankaj Sir & Dr Nisha Bhatnagar Ma'am)	Physical	6.00 pm - 9.30 pm
29.10.2024	Tuesday	Chapter Quiz	IFS Maharashtra - Chapter Quiz on Kahoot	Online Webinar	3.00 pm - 4.00 pm
29.10.2024	Tuesday	Chapter Quiz	IFS Punjab - Chapter Quiz on Kahoot	Online Webinar	5.00 pm - 6.00 pm
31.10.2024	Thursday	SIG	SIG: PCOS	Physical	Half Day
03.11.2024	Sunday	Chapter	Odisha Chapter - 3rd Annual Conference (Dr Pankaj Sir & Dr Shweta Ma'am)	Physical	Full Day
06.11.2024	Wednesday	Chapter	IFS MP Chapter Activity (Polaris)	Online Webinar	5.00 pm - 7.00 pm
06.11.2024	Wednesday	Chapter	IFS Haryana Chapter PCOS Awareness Activity	Physical	Half Day
07.11.2024	Thursday	Zonal Quiz	IFS West Zone Quiz (Gujarat, Rajasthan, Vidarbha, Maharashtra)	Online Webinar	6.00 pm - 7.00 pm
08.11.2024	Friday	Central - YEP	IFS - Young Turks Journal Club - Activity	Online Webinar	7.00 pm - 8.00 pm
09.11.2024	Saturday	Central - UK Forum	IFS UK Forum First Webinar Activity	Online Webinar	6.30 pm - 8.00 pm
09.11.2024	Saturday	Chapter	Bihar Chapter - Jaipur	Physical	12.00 pm - 2.00 pm
10.11.2024	Sunday	Chapter	IFS Chhatisgarh 4th Annual conference	Physical	All Day
10.11.2024	Sunday	Central - NEP	Nursing - Empowerment Program (Nightangle)	Online Webinar	7.00 pm - 8.00 pm
11.11.2024	Monday	SIG + Chapter	SIG: Genital Tuberculosis with MP Chapter Activity	Online Webinar	12.00 pm - 2.00 pm
11.11.2024	Wednesday	SIG + Chapter	SIG: Genital Tuberculosis with MP Chapter Activity	Online Webinar	12.00 pm - 2.00 pm
12.11.2024	Tuesday	Chapter	IFS Kerala Chapter Activity	Online Webinar	7.00 pm - 9.00 pm
13.11.2024	Wednesday	SIG + Chapter	SIG: Endrometrosis with MP Chapter (Sudeeksha 2.0)	Physical	10.00 Am - 2.00 pm
15.11.2024	Friday	Central - EBM	Monthly Meet - Executive Body Meet (EBM)	Physical	5.00 pm - 7.00 pm
16.11.2024	Saturday	North Zone Quiz	IFS Central Zone Quiz (MP, Chhattisgarh, UP West & UP East)	Online Webinar	7.00 pm - 8.00 pm
18.11.2024	Monday	North Zone Quiz	IFS North Zone Quiz (Jammu, Haryana, Punjab & Chandigarh)	Online Webinar	7.00 pm - 8.00 pm
21.11.2024	Thursday	Delhi Quiz	Delhi Central Quiz at R&R Hospital	Physical	9.00 am - 5.00 pm
23.11.2024	Saturday	Chapter	IFS UP East Chapter Activity	Physical	6.30 pm - 8.30 pm
26.11.2024	Tuesday	Delhi forum + SIG	IFS Delhi Forum with SIG Endoscopy Activity	Online Webinar	4.00 pm - 6.00 pm
26.11.2024	Tuesday	Chapter	IFS Kerala Chapter Activity	Online Webinar	7.00 pm - 8.00 pm
28.11.2024	Thursday	Chapter	Chhattisgarh Chapter Activity	Online Webinar	4:00pm-5:30pm
29.11.2024	Friday	Central - Quiz	IFS Quiz - Genius Junction Monthly Quiz	Online Webinar	7.30 pm - 8.00 pm
29.11.2024	Friday	Central - YEP	IFS - Young Turks Journal Club - Activity	Online Webinar	8.00 pm - 9.00 pm
29.11.2024	Friday	Chapter	IFS South Tamilnadu Chapter Activity	Online Webinar	7.00 pm - 8.00 pm
30.11.2024	Saturday	Chapter	IFS MP Chapter 26 Sukanya Awareness Activities (April to Nov)	Physical	Half Day
06-12-2024	Friday	20th Fertivision	IFS - Annual Conference (Day 1) Gujrat	Physical	Full Day

Activity Date	Activity Day	Chapter/SIG / Zone / Joint/ Other	Activity Name	Mode	Time
07-12-2024	Saturday	20th Fertivision	IFS - Annual Conference (Day 2) Gujrat (EBM + GBM)	Physical	Full Day
08-12-2024	Sunday	20th Fertivision	IFS - Annual Conference (Day 3) Gujrat	Physical	Full Day
26.12.2024	Thursday	Chapter	Chhattisgarh Chapter Activity	Online Webinar	4:00 pm - 5:30 pm

Dr Niti Vijay
Director, The Clinics
Senior IVF Consultant, Aveya Fertility,
Pheonix Hospitals

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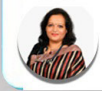

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