IFS
CONVERSATIONS
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Oncofertility

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MESSAGE FROM THE PRESIDENT DESK

Dr Sudha Prasad
President - IFS

Dear Friends,
It is indeed a great privilege and pleasure for me to present the first "IFS Conversation"of our tenure. The sole purpose of getting these conversations is to showcase various recent academic activities conducted by our extremely enthusiastic and committed members spread over 27 chapters across India and abroad.

This time the topic of the conversation is "Onco-fertility". It is a field that bridges the specialties of oncology and reproductive endocrinology with the purpose of maximizing the reproductive potential of young cancer patients. The common cancers in patients of reproductive age in men are Hodgkin's and non-Hodgkin's lymphoma, leukemia, and testicular cancer and in women is breast cancer, thyroid cancer or the cancer of female genital tract. The effective anti-malignancy treatments i.e., surgery, chemotherapy, and radiotherapy have improved the survival rates of cancer patients by up to 70%–90%, making it possible for them to reproduce but may impair or destroy their ability to have children later in life. For women, these therapies can cause ovarian damage that can lead to genetically damaged oocytes, ovarian failure, or other reproductive problems. For men, treatments can similarly cause damage to the testes that interfere with spermatogenesis and testosterone secretion.

As cancer treatments improve and survivorship increases, fertility preservation options in women, men, and children become an increasing important topic. Many treatments such as ovarian tissue cryopreservation or oocyte freezing in females and semen freezing or testicular tissue cryopreservation in males can help in maximizing the future fertility potential.

In the end, I congratulate the editorial team for their excellent hard work and dedication to plan and prepare this news bulletin and wish all readers a very rewarding and pleasant reading. Your feedback and suggestions are always most welcome and sincerely requested.

With best wishes,

Sudha Prasad

Dr. Sudha Prasad

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MESSAGE FROM THE SECRETARY DESK

Dr Neena Malhotra
Secretary - IFS

Dear Members and Friends

"The future cannot be predicted, but futures can be invented". This statement by the Nobel Laureate, Dennis Gabor, is most applicable for researchers in the field of Reproductive Medicine. Over the last half a century, reproductive scientists have unleashed the potential of many technologies and applied them as impactful therapies, including fertility preservation. Given the improved long-term survival of cancer patients there has been growing interest in expanding the reproductive options for these patients. In the era of vitrification, gamete, embryo and gonadal tissue cryopreservation have given hope and the pleasure of parenthood to many of our cancer survivors.

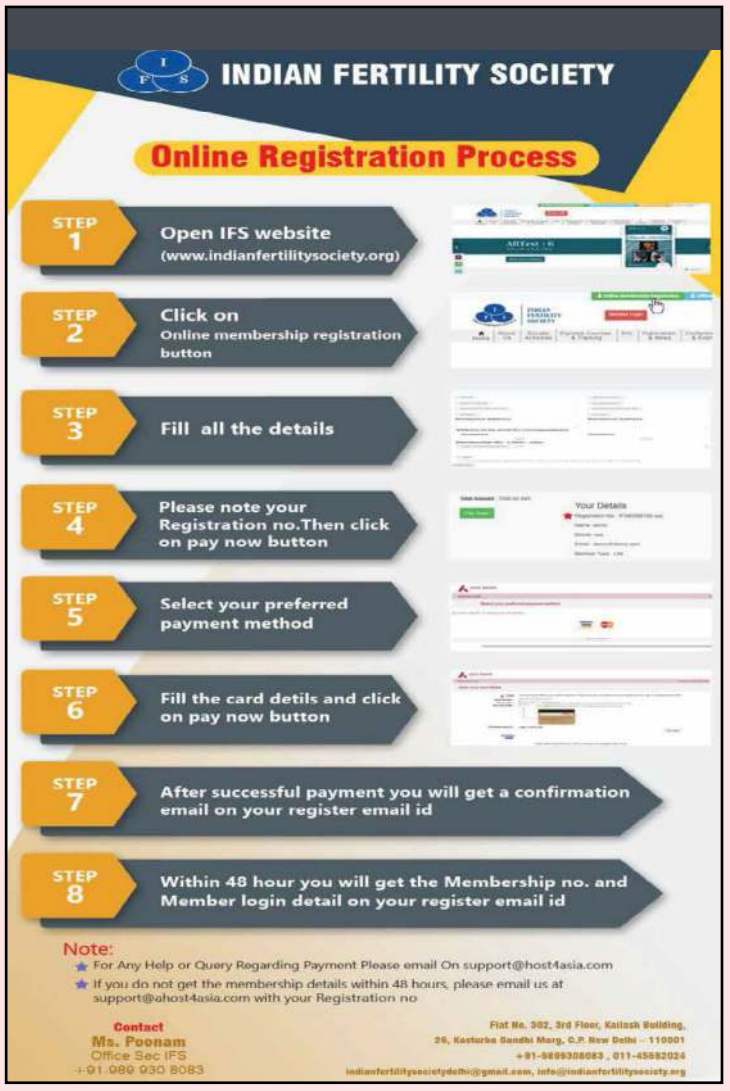
It gives me pleasure to forward the first issue of "Conversation" for my tenure as Secretary General of IFS. While the pandemic may have put a restraint on our clinical work in terms of patient care, the academic activities at IFS have never taken the back seat. This issue of "Conversation" summarizes the fertility-preservation care and provides specific clinical recommendations based on available strategies and technologies for young women with cancer. Besides academics, we give our members a glimpse of activities from IFS chapters and special interest groups over the first quarter.

I would applaud the editorial team, who despite the challenges of the lockdown have been prudent in bringing forth this issue and will continue with the same enthusiasm for the future issues as well.

Best Wishes.

Neena Malhotra

Dr. Neena Malhotra



MESSAGE FROM THE EDITOR'S DESK

Dr. Shweta Mittal Gupta
Editor - IFS

Dr Rashmi Sharma
Jt. Editor - IFS

Dear Members & Friends,

We extend our grettings from the new editorial team of Indian Fertility Society.
Entire nation is facing covid-19 pandemic. Admist this Indian fertility society has taken a lead in continuing academics and medical education.A series of webinars have been organized to benefit all members. IFS has recommended certain guidelines during COVID.

We at IFS are determined to stand up to challenges faced by all of us in view of the lockdown and now when lockdown has slowly been eased out , the challenges will still continue . We will ensure that all relevant academic contents reach all our members through the website. We believe in going green and all our bulletins will be circulated through emails.

This issue of IFS conversation would be giving you all the information of different webinars and journal clubs held. Many of them are still available for viewing and members who missed attending them can take benefit by viewing. This issue is dedicated at onco fertility and are thankful to authors for simplifying complex topic of fertility in cancer patients.

We welcome our members to contribute scientific content in forth coming IFS conversation. We will be more than happy to publish all your academic achievements and awards at national or international level.

Happy reading

Dr. Shweta Mittal Gupta
Editor, IFS

Dr. Rashmi Sharma
Joint Editor, IFS

INVITED ARTICLES

Oncofertility and COVID-19- Dilemmas and Recommendations

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In times of this unprecedented pandemic the world is grappling to understand this novel corona virus disease- COVID 19. In the field of assisted reproduction world over a precautionary approach is being advised for not only the safety of the patients but also for reducing the unparalleled burden on the healthcare system. However, young patients with cancer who are candidates to undergo gonadotoxic chemotherapy and/or radiotherapy need urgent fertility preservation to complete their families following cancer treatment completion even in this pandemic.[1,2] Teamwork with shared decision making between the oncologists, anaesthetists, fertility specialists and the patient is cardinal.

New Challenges in COVID Era:

This unique pandemic has challenged the world at every level. Medical guidance is ever changing and with these uncertainties lie the challenges that both the patients and doctors face. The patients can face hurdles that can be as basic as getting to the tertiary hospitals units that offer both cancer care and fertility preservation treatments to more complex emotional thoughts dealing with the fear of both the known and unknown risks of complications from the COVID 19 virus during cancer treatment to the additional fertility preservation treatments involving further hospital visits and in some units additional costs relating to COVID testing and PPE gear.[3]

Moreover, the anxieties from fear of contracting the virus during hospital visits leading to isolation and quarantine are real for some to even consider opting out of fertility preserving treatments whilst fighting their most basic desire to procreate.

For the healthcare providers the novel challenges of providing safe and optimal care albeit dealing with the undefined risks remain.

Nonetheless, where resources allow, with extra caution and strict adherence to the COVID 19 safety protocols and local guidelines oncofertility is a feasible option giving hope for new life in future. Hence, we urge the oncologists and the oncofertility specialists to consider fertility preservation and work as a dedicated team to support these young cancer patients optimize their future fertility and reproductive health even in this pandemic Practical Tips and Recommendations-

1. Patients should discuss with their oncologist and oncofertility specialists the wish to have children following treatment completion and if it is possible to safely balance this option without compromising their cancer care and further increase the risk of infections by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

2. Outline various fertility preservation procedures that can be undertaken safely with all the precautions recommended by various national and international organizations including having protected pathways. [4]

3. Detailed oncofertility counseling should clearly discuss the additional concerns including the during COVID-19 outbreak whist defining all the established safety protocols in place to minimize these risks.[4]

4. Specific SOPs and consents to be taken detailing all known and unknown risks including possibility of cycle cancellation if patient becomes symptomatic for COVID.[4]

5. Implement a disaster plan and preferably where possible having two working teams that should alternate eg Team A-Fertility specialist A, Nurse A, Anaesthesiologist A, Embryologist A and Witness A with a similar Team B so in the event Team A comes in contact with an infected patient then the other team can take over.[5]

6. Triaging these patients for the SARS-CoV-2 testing in accordance with the local guidelines before starting any ART procedures.

7. Reassure the patients that currently the risk of viral contamination in in vitro fertilization laboratories to sperms/eggs/embryos/ovarian tissue from the patients or the healthcare workers can be considered low.[5]

8. Current laboratory recommendations suggest separate tanks for freezing of the sperms/oocytes/embryos/ovarian tissue as per local guidelines.[5]

9. Consider temporary ovarian suppression with GnRH agonists during chemotherapy where feasible as an option to protect ovarian function during treatment.

10. Ovarian tissue cryopreservation in patients that cannot wait 2-3 weeks before starting anticancer treatments can be proposed although this is an experimental procedure that will need surgery, hence the pros and cons need careful reviewing especially in this pandemic.
11. Ovarian transposition can be considered before starting pelvic radiotherapy, however this again will need surgery, hence the pros and cons need careful discussion and planning.
12. ART units to maintain a separate log of cases done in this pandemic and share experiences to learn from one another.
13. Provide psychological support to both the patients and the healthcare staff.

In conclusion, advances in oncofertility have given lot of hope to preserve future fertility and it should be considered where resources allow even in this pandemic.

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Protocols for Controlled Ovarian Stimulation in Fertility preservation

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Outline of the article

Introduction
Physiology
Protocols
Conventional
Random Start
Dual Stimulation
Challenges faced during stimulation Other methods of fertility preservation Key message

Introduction

Women of reproductive age diagnosed with cancer are often interested in preserving gametes or reproductive tissue that would allow for future genetic parenthood. Preservation of fertility is often accomplished in young cancer patients via ovarian stimulation followed by oocyte or embryo cryopreservation.

Conventional stimulation protocols, however, require 2-4 weeks to complete ovarian stimulation, oocyte retrieval and possible fertilization. Such a strategy may not be feasible in patients requiring urgent cancer treatment. Recent studies have highlighted that random start ovarian stimulation can be initiated irrespective of the phase of the menstrual cycle and is an attractive alternative to conventional ovarian stimulation. The primary aim of the current review is to discuss the various available protocols for controlled ovarian stimulation in patients undergoing fertility preservation prior to oncotherapy.

Physiology

A detailed analysis of the menstrual cycle has clearly shown that most of the women in the reproductive age group, to the tune of 68% would exhibit two waves of folliculogenesis. The rest 32 % of the women ,indeed showed 3 cycles of follicular maturation during their inter ovulatory Interval(the period between two successive ovulations, beginning in the post ovulation phase till the next ovulation taking place). It was further observed that none of the regular ovulating healthy young adults had only a single wave of follicular growth. These waves were further classifies as major and minor . In the major waves a dominant follicle was selected for preferential growth at the expense of subordinate antral follicles. Whereas during the minor waves there was no selection of the dominant follicles .

Utilizing this concept, various protocols for ovarian stimulation have been studied . This is more helpful in patients with oncofertility issues where we need to maximize the outcome in minimum available times[1-3].

Conventional Protocols

The conventional protocols usually take ranging from 2-4 weeks for ovarian stimulation and subsequent retrieval . Newer protocols have been designed to address the lack of time without any negative effects on the overall quality of the gametes. They are most commonly used in cases of patients undergoing oncotherapy.

Conventional Ovarian stimulation protocols

Amongst the conventional start protocols , the Gnrh (Gonadotropin releasing hormone) antagonist protocols are the preferred as compared to the long agonist protocol for ovarian stimulation, where the duration from start of suppression to the oocyte retrieval would vary from 4 to 6 weeks

In Gonadotropin Agonist protocol the ovarian stimulation is started on day 2 of the menstrual cycle. Followed by Gnrh Antagonist either on day 7 of hormones or when the leading follicle reaches 12 to 14 mm. This Gnrh antagonist prevents premature ovulation and is administered till the trigger is given followed by retrieval of oocytes.

Disadvantages The patient needs to wait till day 2 for start of stimulation.so the time interval between the diagnosis of malignancy and oocyte retrieval becomes significantly longer.

Advantages This is the most widely studied and used protocol across the world. During the antagonist cycle if an agonist is used as a trigger, the risk of ovarian hyperstimulation can be majorly reduced.

Random start Protocols

One of the most commonly used protocols in patients undergoing fertility preservation on oncotherapy.

The main principle of using this form of protocol is the utilization of multiple waves of folliculogenesis.

The menstrual cycle is divided into the late follicular phase which is around day 7 of the menstrual cycle which was characterized by the presence of a dominant follicle (>13 mm) and progesterone level <2ng/mL.4

Stimulation in the early follicular phase

Early follicular phase would mean stimulation in patients with all the follicles lesser than 10 mm diameter.

This resembles the conventional stimulation where the gonadotropins are administered alone till the leading follicle reaches 10 mm. Once the lead follicle reaches 12 mm , we introduce the Gnrh antagonist and continue both drugs till the time Hcg (Human Chorionic Gonadotropin) is administered as a ovulation inducing trigger. Hormonal assessment of Estradiol and Luteinizing hormone would help to assess any premature luteal rises and guide the dose of gonadotropins to be administered.

Stimulation in late follicular phase

This comprised of a group of patients who had the leading follicle more than 10 mm to 12 mm in diameter. In this case the GnRH antagonist was started along with the gonadotropins for follicular stimulation. This was continued till three or more follicles reached 18 mm, subsequent to which a trigger with Human Chorionic gonadotropin was administered for follicular maturation.

Stimulation in luteal phase

The luteal phase is defined as the post ovulation phase of the menstrual cycle.in the second half of the cycle . The luteal phase was determined by progesterone level >3 ng/ml. In cases when the patient reports at the periovulation period, ovarian stimulation is started in the post ovulation phase. A baseline evaluation of the hormonal levels will help us to assess the degree of suppression required before the actual stimulation is started. It can be started the very next day or after one or two days.

In the initial phase Gnrh Antagonists may be administered in Luteolytic doses, so as to supress the increased progesterone levels in the post ovulatory period. The initial higher dose may be followed by normal doses of Gnrh which is 0.25 IU in case of Cetrorelix and Granirelix. Stimulation with recombinant FSH can be started on day 2 or 3 of the Gnrh antagonist and continued till the time of trigger for oocyte maturation and retrieval comes5.

In Luteal halt protocols, a higher dose of Gnrh Antagonist (3 mgs single) or 250 mcg daily multiple doses may be required for bringing down the Estradiol levels to below 60pg/ml.6 Once the desired levels are achieved then the stimulation could be started with Recombinant FSH followed by GnRH antagonist at the follicular sizes of 12 to 14 mm.7 This would subsequently be followed by a trigger at 18 mm size of the follicles.

Random Stimulation protocols with IVM

In Vitro Maturation or IVM refers to early aspiration of the immature oocytes as an earlier stage that the conventional gonadotropin stimulation8. These oocytes which are aspirated, undergo maturation In Vitro, before being subjected to IVF or ICSI9

Advantages of Random start protocols
The main advantage of this protocol is the flexibility to start stimulation at any phase of the cycle. The major superiority arises from the fact that the overall fertilization and pregnancy rates are similar to the conventional protocols for IVF.

Disadvantages of Random start protocols
More research is needed to support Random start protocols with IVM for it to be freely used in oncofertility preservation regularly.

Dual Stimulation Protocol

This is a type of random stimulation antagonist protocol, more applicable in patients who are about to undergo oncotherapy, and want to maximize their fertility potential. The patient undergoes two cycles of stimulation during the entire menstrual cycle.
The first cycle is started on day 2 or 3 of the cycle like a regular antagonist cycle. The patient is monitored with regular transvaginal ultrasound and accordingly the dose of gonadotropins is decided as in a conventional protocol. The GnrH antagonists are added when the follicles reach a size of 12 mm.
Trigger with HcG is given at a follicular size of 18mm.
The follicles are aspirated and oocytes are collected.
The second cycle of stimulation is usually started either on the same day post aspiration or
Depending on the response of the ovary
On the day of oocyte collection, the patients are started with the second cycle of stimulation.
Gonadotropins can be recommenced either on the same day, or after a few days for those patients who wished to take a break for a couple of days. The dose of gonadotropin is usually similar or slightly increased according to the response to stimulation in the first cycle.
Patient is regularly called for transvaginal ultrasound examinations and subjected to hormonal evaluation to decide on the dose of the gonadotropins. The follicles which have been aspirated out in the first cycle of retrieval are excluded from the count. Once t a follicular size of >17 mm is attained, a trigger with HcG is given followed by oocyte retrieval.

GnRH antagonist and or an aromatase inhibitor is usually continued for a period of 1 week till the blood estradiol levels reduce. The decision for second triggering and oocyte retrieval was made based on the follicular growth (three follicles >17 mm).
Following the second oocyte retrieval, all patients continued GnRH antagonist for 1 week, and those with estrogen receptor positive breast cancer were also continued on an aromatase inhibitor.

Other methods of Fertility preservation

Apart from Embryo and oocyte cryopreservation, various other methods have been studied and applied with varying degrees of success.

Methods like surgical ovarian transposition, pelvic shielding during radiation have been used with great degrees of success.

Ovarian Tissue cryopreservation and grafting are applicable in pre-pubertal age groups where the cortex of the ovary is cryopreserved and subsequently thawed at a later date,
This method is usually not applicable in haematological malignancies as there is a risk of transmission of malignant cells.
In Vitro maturation is another method, which is being utilized in many centres and is more applicable in the scenario of fertility preservation. This method the follicles are aspirated before the oocytes undergoes maturation. Subsequently, they are matured and fertilized in the media

Challenges in Ovarian stimulation in oncofertility

There are various challenges faced by the treating clinician, when we consider fertility preservation in cancer . One of the major concerns is the lack of time, which the clinician is juggling with, in order to maintain a balance between maximizing the fertility potential without delaying the oncotherapy.

Cancer may is state of increased catabolism, stress, and malnutrition, which may result in adverse effects various organ systems. There is a direct correlation of stress and hypothalamic dysfunction.10 The response to the gonadotropins used in stimulation would be suboptimal in cases of stress induced hypothalamic disability.
Apart from the poorer response to gonadotropins, detrimental effects have also been shown on ovarian reserve and oocyte recovery at retrieval procedures.11

Amongst the patients with cancers of breast a few studies have shown a risk for DNA damage, resulting from BRCA gene mutations.12
Indeed a meta-analysis demonstrated a statistical significance when comparing the number of retrieved oocytes for those in the cancer group compared to controls: 11.7±7.5 vs. 13.5±8.4, p=0.002 (95% CI, −2.976; −0.621).11 It was observed that the oncology patients showed a significantly lower oocyte retrieval and higher cancelations as compared to healthy age matched controls11,13.

A few studies have shown that overall response to ovarian stimulation is poorer in patients with hormone-dependent cancers as compared to non-hormone-dependent cancers 14.
In patients with estrogen sensitive cancers, it is very important to start the patients on estrogen suppressing aromatase inhibitors, so as to maintain low levels of estrogen during the entire phase of stimulation with gonadotropins.
Letrozole and Tamoxifen are the two drugs which have been used for their antiestrogenic effects for gonadotropin stimulation. Although a few studies have claimed the superiority of Letrozole, but larger studies need to be performed to reach to definitive conclusions.
These drugs may also be continued in the post oocyte retrieval phase for a few days till the serum estradiol is maintained at lower levels.

There is an increased risk of thromboembolism in these patients. Apart from the hypercoagulability dur to malignancy the supraphysiologic serum E2 levels also increase the risk of such phenomenon taking place.15
These patients should be ideally co administered with anticoagulants, such as low-molecular-weight heparin to prevent such a risk.16

The patients undergoing fertility preservation are more likely to have neutropenia and are prone to develop infections. These patients are candidates for antibiotic administration during the invasive procedures of oocyte retrieval.

The doses of gonadotropins used in these patients is on an average higher than the younger healthy adults. Subsequently there is an increased risk of Ovarian Hyperstimulation Syndrome amongst these patients.

Use of agonist trigger, aromatase inhibitors and symptomatic management in these patients is the mainstay of management in these cases.

Key Message

Fertility preservation is a well-established field of reproductive medicine which should be offered to all patients undergoing gonadotoxic oncotherapy. The phase of the cycle does not alter the initiation of stimulation. Random start protocols provide excellent opportunity to stimulate and obtain oocytes or embryos for preservation of fertility in appropriate patients.

Table 2: Late follicular phase Initiation

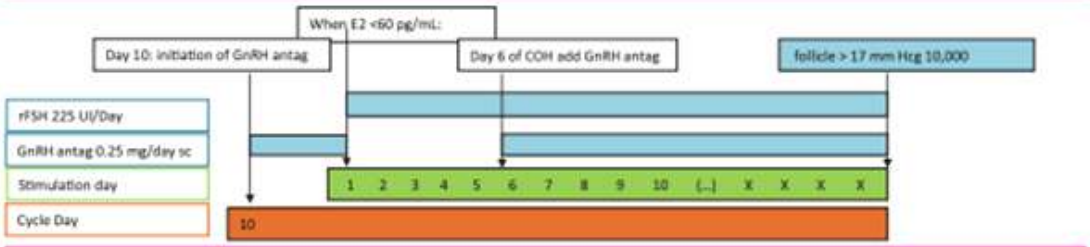


Table 3: Early follicular phase Stimulation

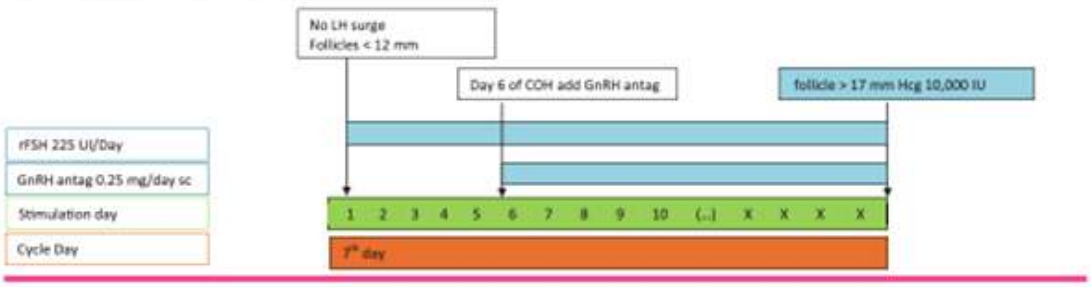


Table 4: Luteal halt Protocol

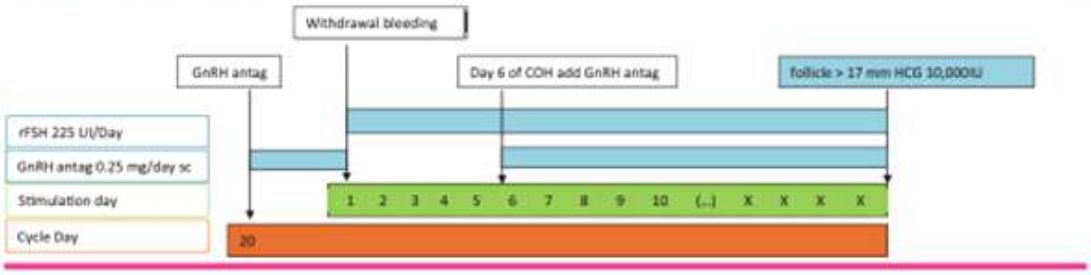
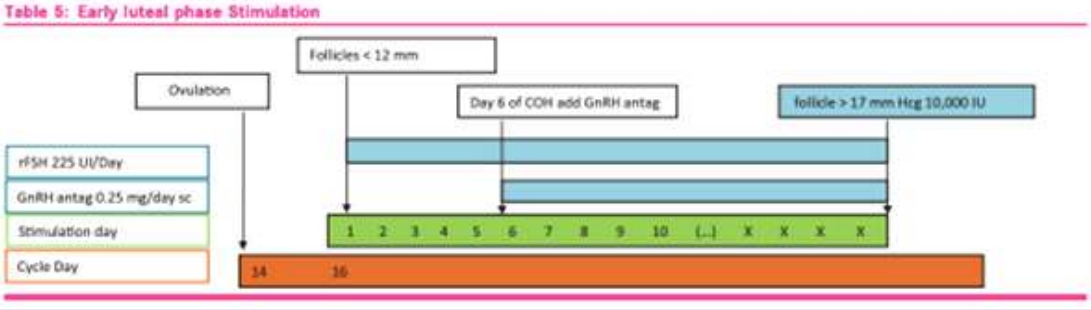


Table 5: Early luteal phase Stimulation



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Fertility Preservation in Borderline ovarian tumor in unmarried girl

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Abstract
Fertility sparing surgery in form of bilateral ovarian cystectomy was done after ruling out tuberculosis in a 23 year old unmarried girl with large bilateral adnexal masses on MRI. She was admitted with C/O pain in right iliac fossa and weight loss since two months. Histopathology of Right side ovarian cyst revealed mucinous borderline ovarian tumour (BOT). These are tumours of low grade malignant potential with high rate of relapse and need close follow up.

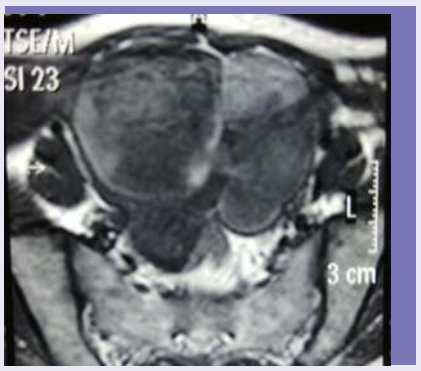
Introduction: Borderline ovarian tumour (BOT) constitutes approximately 15 % of all epithelial ovarian cancers.80 % of them are detected at stage 1. They occur predominantly in women < 40years. Most Common types are serous (53-65%) and mucinous (32-42%) and 10-year survival rate is more than 95 %.1 Fertility-sparing surgery is done in young cases with early stage BOT.

Case Presentation: 23years unmarried girl presented to the Gynae OPD with C/O pain in right iliac fossa and weight loss since two months. She had regular menstrual cycles. No H/O tuberculosis.General condition was fair, vitals were normal.No lymphadenopathy, thyroid and breast were normal.Chest &CVS- NAD.On per abdomen examination- A 15x10 cm abdomino-pelvic mass, cystic in consistency with restricted mobility, non-tender with smooth surface and slightly irregular margins was felt.On P/R examination- two separate masses one approx 10x8 cm was felt in the left adnexal region, another mass 5x5 cm approx was felt in the right adnexa with restricted mobility.Both the masses were non-tender and of cystic in consistency. Uterus was normal size. Rectal mucosa free.On investigation Tumour markers-CA 125-- 130 U/ml was raised. MRI Abdomen and Pelvis revealed-Bilateral adnexal large encapsulated multiloculated solid, cystic masses closely abutting each other. Solid components were seen as papillary projections along the septae and walls of locules. Contents were hypointense on T2WI and isointense on T1WI.Scanty, compressed ovarian parenchyma was seen along periphery of both masses,findings were suggestive of neoplastic changes. Surgical staging followed by fertility sparing surgery which included bilateral ovarian cystectomy with preservation of normal ovarian tissue and uterus was done. Histopathology of Right side ovarian cyst revealed mucinous borderline tumor. Left side ovarian cyst report was benign mucinous cystadenoma. Omental biopsy showed noninvasive implants.
After 6 weeks of follow up CA125 was 50U/ml and after 12 weeksCA 125: 22 U/ml.Follow up Ultrasound & MRI Abdomen and Pelvis done at 12 weeks were normal.

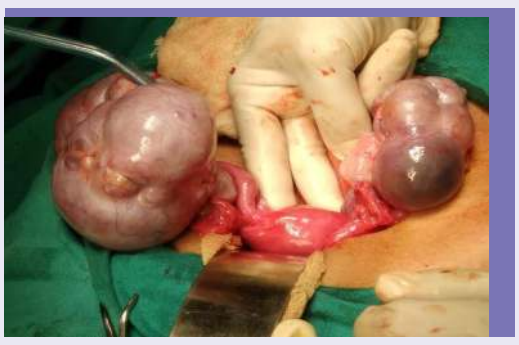
DISCUSSION
The entity of BOT was recognized by Taylor in 1929 as semi-malignant. 1
It is diagnosed by definitive criteria :
1. Epithelial proliferation with papillary formation and pseudostratification.
2. Nuclear atypia & increased mitotic activity. (Not > 4 mitoses per 10 hpf).
3. Absence of true stromal invasion.
The most common presentation is lower abdominal or pelvic pain. The case may be asymptomatic and incidental adnexal masses may be diagnosed on routine ultrasound.2
Surgical staging followed by USO should be considered as the first choice of fertility-sparing treatment for BOTs in women wishing to preserve fertility.3 Bilateral ovarian cystectomy is the treatment of choice in young patients with early stage BOTs in which uterus and ovarian tissue in one or both ovaries are preserved. Although there is concern of increase recurrence rate with cystectomy as some malignant tissue may be left in situ the rate of recurrence between u/l salpingo-oophorectomy (USO) and ovarian cystectomy did not differ significantly.[4] The most common site of recurrence is remaining ovary and recurrence after conservative surgery is borderline in most cases. The recurrence rate in the fertility-sparing surgery does not differ significantly by type of surgery, therefore, cystectomy can be considered for patients with bilateral tumours or previous USO. Rate of recurrence of BOT is 7% as compared to radical surgery group(5%) with no statistically significance. [5]
Even advanced-stage BOTs with non-invasive implant can be safely treated with fertility sparing conservative surgery. With invasive implants fertility-sparing surgery could be considered, but with an individualized approach.[6]
Although laparotomy is the usually performed, laparoscopic techniques have been used by skilled surgeon. The concerns over implementing laparoscopy for BOTs are risk of tumor rupture during surgery approx.70%, port site metastasis and decrease survival rate due to failure to thoroughly define the surgical stage.The advantages are lower morbidity rate and less frequent adhesion (important for infertility cases). Standard radical surgery is indicated in women>40 years and whose child bearing is completed. It includes exploration of abdominal cavity, peritoneal washings,total hysterectomy with bilateral salpingo-oophorectomy (BSO), infracolic omentectomy and resection of macroscopic suspicious lesions.
Since recurrence is high during first 2 post op years, so regular follow up of cases of BOT for up till 2 years is very important. According to NCCN 2017, follow-up tests and schedule is advised every 3 to 6 months for 5 years. It includes physical and pelvic examination, CBC,tumour markers as Ca-125,Ultrasound,CT/MRI of chest,abdomen and pelvis/PET CT as needed.5 The prognostic factors are stage of the tumour ,invasive implants and micropapillary pattern.[7]
Spontaneous pregnancy rate of 32-65% has been reported in BOT treated with fertility sparing surgery with a mean duration 15 months. 3,8

Role of Ovarian Cryopreservation in BOT:
Donnez et al (1998) proposed cryopreservation of contralateral ovarian cortex biopsy at first-look laparoscopy if the borderline nature of the tumour is suspected before surgery [9]
Careful selection of candidates for this kind of treatment is necessary and close follow-up is required. Although it as a potential option the disadvantage is retransplantation exposes patients to the potential risk of transplantation of borderline cells. In vitro maturation of retrieved oocytes followed by vitrification and cryopreservation of immature oocytes from fresh tissue or follicular aspirates are other options.

Conclusion: Fertility-sparing surgery in form of ovarian cystectomy should be considered for young women with one ovary or with bilateral tumours with no invasive implants with regular close follow up.



MRI : showing relatively iso to hypointense components with solid hyperintense components



Intraop findings showing B/L irregular bosselated adnexal masses

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Fertility Preservation in Breast Cancer

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Introduction-

Breast cancer is the most common invasive cancer that accounts for one third of all neoplasms seen in reproductive-age women and affects tens of thousands of women each year in that age group and also the leading cause of death from cancer among women. In 15–25% of cases, patients are premenopausal at the time of diagnosis, and about 7% of them are below the age of 40. Therefore, a considerable amount of young women are diagnosed with breast cancer during their reproductive life. Despite high incidence rates survival rate of women diagnosed with breast cancer is nearly 90% in western countries and developed Asian countries. The diagnosis of any type of cancer makes a life crisis for any person as it impacts physical, social and emotional resources of the patient. Younger patients face the additional potential loss of reproductive function which in turn impacts their future fertility. It is important to appreciate the differences between breast cancers in young and older women. With increased cancer survival rates, it is important that attention should be given to post treatment quality of life for patient and timely fertility preservation helps in adding a lot to quality of life of such women.

Effect of cancer treatment on fertility -

Many of the chemotherapic agents used for treatment of breast cancer have gonadotoxic impact in females . All chemotherapeutics, irrespective of their action mechanism, can damage developing follicles by interrupting granulosa cell development, which subsequently causes amenorrhoea. However, the degree of permanent damage to ovarian reserve depends upon age of patient, prior ovarian reserve of patient, type of chemotherapeutic agent used and duration of overall treatment. Alkylating agents such as cyclophosphamide and ifosfamide are particularly notorious for their deleterious effect on ovarian function. Rate of amenorrhea is higher in higher age group women as compared to younger age women.([1],[2],[3])

It is important to consider that only amenorrhea should not be taken as indicator of gonadal damage in women who underwent chemotherapy, as even in women who resumed menses following chemotherapy there is significant impact on their ovarian reserve. Also, hormone therapy in breast cancer can lead to amenorrhea without indicating permanent damage to ovarian reserve. So, a combination of AMH and AFC along with clinical evaluation should be utilized while giving fertility care to such women.

Importance of early referral to fertility specialist -

The combination of above-mentioned factors justifies the importance of fertility preservation and reproductive counselling at the time of breast cancer diagnosis in women. Early referral to reproductive specialist helps in giving sufficient time to patient for decision making regarding type of fertility preservation, that she wishes to choose. There have been recent new advances in the field of fertility preservation techniques, which is like a ray of hope in darkness for many of the breast cancer survivors.

Fertility preservation techniques for patients of breast cancer -

The various fertility preservation techniques available for a patient of breast cancer are

1. Cryopreservation of embryos or oocytes
2. Cryopreservation of ovarian tissue
3. Ovarian suppression with GnRH agonist
4. Immature oocyte retrieval and in vitro maturation

Cryopreservation of embryos or oocytes -

If a patient can afford 2-3 weeks' time prior to start of chemotherapy, then either embryo or oocyte cryopreservation is the most well-established fertility preservation technique for such women. The procedure for both remains similar as used in standard IVF protocol involving approximately 10-12 days of ovarian stimulation with the help of gonadotropins and antagonist followed by oocyte maturation trigger with GnRH agonist and oocyte retrieval after 34-35 hours later. The only differences in ovarian stimulation between a routine infertility patient and cancer patient are two –

1. Use of random start protocol
2. Use of concomitant letrozole

According to the recent discovery the stimulation protocol can be started with random initiation regardless of the day of menstrual cycle as there are multiple waves of follicular recruitment throughout the length of cycle. This saves crucial time as we do not have to wait for initiation of menstruation for starting stimulation(4). Also it has been demonstrated that the number of oocytes retrieved is not affected by the timing of start of ovarian stimulation (whether proliferative phase or luteal phase)(5,6)

The problems associated with embryo and oocyte cryopreservation are firstly 2-3 weeks' time needed prior to chemotherapy and secondly high levels of estradiol secreted from developing follicles , which may be harmful for hormone sensitive cancer . Letrozole has been utilized along with standard gonadotropin stimulation to keep the systemic levels of estrogen low throughout . Letrozole is an aromatase enzyme inhibitor preventing formation of estrogen . So while multiple follicles form due to gonadotropin stimulation ,estrogen levels remain similar to those found in a normal menstrual cycle without affecting the overall oocyte yield.([7],[8])

Embryo preservation has long been considered established technique of fertility preservation ,however in post pubertal females without a male partner oocyte cryopreservation may be considered . With refinement of cryopreservation and thawing techniques ,oocyte cryopreservation is no longer considered experimental and has been approved for routine clinical use . recent studies have reported that embryo transfer cycles using frozen-thawed oocytes had comparable success rates to those using unfrozen oocytes.([9])

Oocyte cryopreservation along with embryo may also provide more autonomy to women in case of future separation from partner . So oocyte cryopreservation should also be discussed with women in committed relationship.

Cryopreservation of ovarian tissue -

If a breast cancer patient does not have time to undergo ovarian stimulation prior to chemotherapy, ovarian tissue cryopreservation may be offered. Although more than [80] livebirths have taken place with the use of ovarian tissue cryopreservation and auto transplantation , the technique is still considered experimental([10]).

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In-vitro maturation (IVM) of oocytes -

Retrieval of immature oocytes after minimal or no gonadotropic stimulation and hCG priming or exvivo from ovarian tissue offers the advantage of initiating cancer treatment without delay . However the technique of IVM is still experimental with very few live births reported in PCOS patients and only [1] live birth in cancer patients reported recently in April 2020 (16,17,18).

The in vitro maturation of primordial follicles from either in vivo extraction of follicles or ex-vivo from cryopreserved ovarian tissue holds enormous potential for future but needs to overcome lot of technical hurdles before coming in to routine clinical practice . Utilization of primordial follicles from cryopreserved ovarian tissue ex vivo also negates the possibility of reintroduction of malignant cells following auto-transplantation of cryopreserved ovarian tissue .

Conclusion -

With improving survival rates in young patients with breast cancer , it is imperative to provide reproductive counselling to patients before starting chemotherapy . Early referral to a reproductive specialist is very important to provide enough time to patient for decision making. Embryo and oocyte cryopreservation following random start ovarian stimulation with gonadotropins and Letrozole co treatment is the most accepted method of fertility preservation in such patients . However patients who cannot afford a delay of [2] -[3] weeks prior to chemotherapy, may be offered ovarian tissue cryopreservation with subsequent auto transplantation . Use of GnRH agonist suppression of ovarian function has been reported with encouraging results recently . In Future , the technology of IVM holds promise with recent report of [1] live birth in cancer patient.

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IFS ACTIVITIES 2020

VIBRATE MEETINGS

INVESTIGATING INFERTILE COUPLES-WHAT, WHEN AND HOW

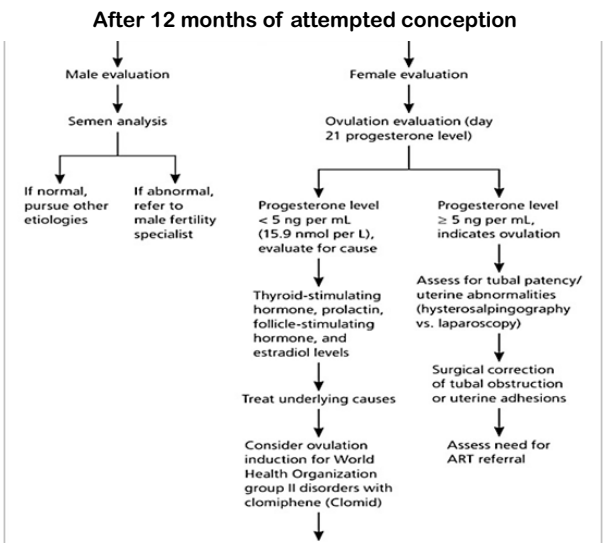
Date: 28 April, 2020

Name of the activity :Vibrate

Speaker: Dr Sudha Prasad- President IFS

Infertility is defined as inability to conceive after one year of regular unprotected intercourse (6 months if female partner is >35 years).It affects 13-15% of couples. Probability of conception for a healthy young couple is 20-25% per cycl , 80-85% couples conceive by the end of first year. Basic questions to be kept in mind while investigating a couple are: whether semen parameters are normal, is female partner ovulating and her ovarian reserve. Is the endometrium clinically suitable and look for added pelvic pathologies like fibroids, ovarian cyst, Aadenomyosis

Algorithm to investigate infertile couple



IFS ACTIVITIES 2020

VIBRATE MEETINGS

MALE INFERTILITY-CASE FILES

Date: 12 May, 2020

Name of the activity :Vibrate
Speaker: Dr Abha Majumdar
Male infertility; commonly encountered problems by gynaecologist

Questions faced by gynaecologist while treating infertile couples with semen abnormalities.

1. **What is the effect of duration of abstinence before semen testing done?**

   The ideal abstinence interval suggested by World Health Organisation (WHO) before semen is given for testing is between 2 to 7 days. There is some impact of ejaculatory abstinence on semen analysis parameters which has been reviewed in various studies. It has been seen that longer abstinence is associated with increase in semen volume and count. However, effect of abstinence or motility, morphology, and DNA fragmentation rate are contradictory and inconclusive. Nevertheless, a trend appears towards improvement in these para metres with shorter abstinence. It is also important to note that the first fraction of an ejaculation is the most effective part for conception as the sperms are more numerous, move more and present better-quality DNA than those which come through the second ejaculate. Even in men suffering from an-ejaculation (it is the pathological inability to ejaculate in men with or without orgasm) first ejaculation obtained by electro ejaculation is much better than the quality of the second electro ejaculation. Therefore, it is obvious that repeated procedures of sperm collection by electro ejaculation are not justified for improving the sperm quality in an-ejaculatory neurologically intact men.

2. **Two labs show different semen analysis reports of the same person. How to identify correct report? What is a normal semen analysis report?**

   When we see several different reports from good laboratories it may become difficult to decide which report to believe as correct. This becomes more important if one report shows normal semen parameters and the other sub-normal. It is important to note what is written in the column of morphological characteristic of sperms. Generally, more than 4% of normal sperms constitute a morphologically normal semen sample. If we find a technician who has reported 80% of normal forms or even 30% of normal sperms it indicates that the technique of doing the semen analysis is not the standard technique or the technician is not trained adequately to do a semen analysis. Most of the laboratories have technicians who have good experience in blood and urine testing but are very poorly trained regarding semen analysis which is quite different from the above two. Mostly technicians working in fertility centres which offer semen analysis, are more proficient in the assessment of semen samples. A beautifully typed report from a leading laboratory does not qualify the report to be correct.

   Normal semen analysis which was redefined by WHO in 2010 shows differences from the standard semen para metres which were followed earlier ever since the reference values were defined by WHO in 1998. The semen volume from 2 ml to 1.5 ML is now considered normal, sperm concentration of 15 million/ml from 20 million/ml and progressive motility now of 32% instead of 50% is now redefined by WHO as normal. Sperm morphology 4% or above is considered normal and is generally not above 14% to 20%.

3. **Ultrasound report shows the diagnosis of varicocele with subnormal semen report. What should be advised?**

   Whenever an infertile couple comes, and the man carries a semen analysis report which shows mild oligo-astheno-terato-zoospermia (OATs) along with an ultrasound report showing grade 1 varicocele how should we proceed. If the varicocele is only demonstrated by ultrasound on standing and coughing and not palpable clinically then it is grade 1, and a case of subclinical varicocele which is defined as a non-palpable enlargement of the venous plexus of the spermatic cord which can be diagnosed only by imaging techniques. No surgical repair is recommended in such case, as studies have shown that, there is no increase in the sperm parameters nor in the pregnancy rate post operatively. Diagnosis of varicocele which is can easily be made by physical examination of scrotal palpation in upright position or in lying down position is truly clinical varicocele and comes under grade 2 and 3 respectively. These are the cases which may sometimes benefit from surgical varicocelectomy hence needs to be referred either to a urologist or infertility/IVF specialist.

4. **How to proceed if azoospermia reported in a semen analysis report and when to refer such cases?**

   Azoospermia is defined as 'absence of spermatozoa in the sediment of a centrifuged semen sample of a man' and crypto-zoospermia is as 'extremely low spermatozoa concentration (≤1 million/mL) in the ejaculate of a man' according to WHO. These situations are generally diagnosed during a routine male infertility investigation. Azoospermia is seen approximately in 1% of the male population and may be as high as 20% among male infertility cases.

   The first thing to be noted from the semen analysis report is the volume of the semen. If this is found lower than normal one needs to rule out history of spillage of the sample while collection. If there has been no history of spillage, the pathological causes of low semen volume are many, such as retrograde ejaculation, an-ejaculations, and hypogonadism. Even anatomical causes contribute to low semen volume such as ejaculatory duct obstruction or congenital absence of the vas/seminal vesicles which can be ruled out by further investigations, for which the man needs to be referred to a urologist/andrologist. If this was not the case, then a repeat semen analysis is recommended after 7 days requesting the laboratory for centrifugation of the sample. If we find sperms in the sediment this is possibly a case of crypto-zoospermia. All these cases of azoospermia or crypto-zoospermia need further investigations and should be referred to an ART clinic.

5. **Can we treat obese men medically with low sperm counts with sexual dysfunction?**

   Obesity is a possible cause of secondary hypogonadism associated infertility in some men. The mechanism by which this happens is as following. Enzyme aromatase is highly expressed in peripheral fat tissue and converts testosterone to oestradiol, causing increased peripheral oestradiol production. High levels of oestradiol inhibit secretion of LH and FSH from the pituitary by negative feedback mechanism. Reduced levels of LH and FSH in turn lead to a reduction in testosterone synthesis and sperm production leading to infertility. To counteract the physiological effect of elevated oestradiol, use of aromatase inhibitors have seen to normalise serum testosterone by stopping its conversion to oestradiol thus its effect on spermatogenesis. The commonly available aromatase inhibitors available are letrozole which is used in doses of 2.5 mg/day or anastrozole given in the doses of 1 mg/day for a period of 3 to 6 months. Generally, with the use of aromatase inhibitors the serum oestradiol levels fall, and the total testosterone levels increase and so does sperm concentration.

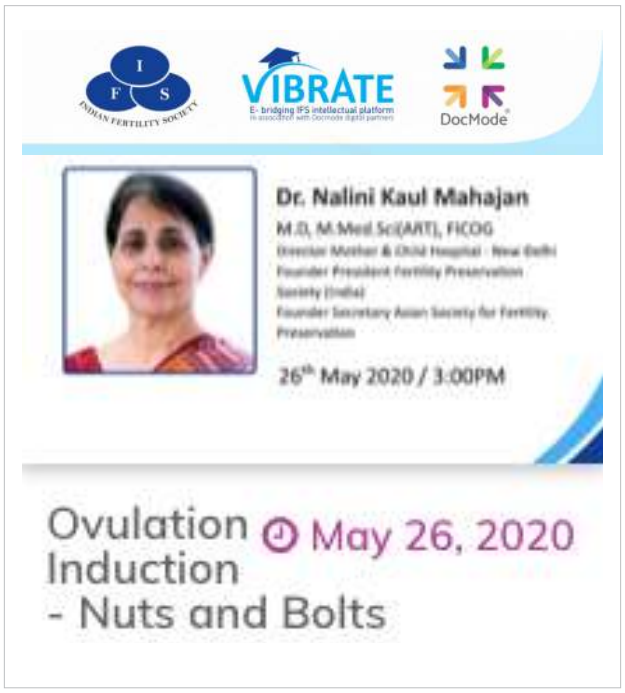
6. **What is the role of available antioxidants in treating low semen para metres in infertile men?**

   Antioxidants are extensively used in the treatment of subnormal semen para metres in male subfertility. There are many vitamins and micronutrients used as antioxidants in practice. One of the most used antioxidants is vitamin C which is found in abundance in the semen of fertile men. It is known to protect sperm's DNA from free radical damage by virtue of which it improves sperm quality. It is given in doses of 1000 milligrams per day orally for 3 to 6 months. Vitamin E protects sperm cell membrane from damage therefore improve sperm motility and is used at a dosage of 600 mg per day for 3 to 6 months. Other micronutrients like selenium is used as 200 µg a day, glutathione 400 mg per day, and L-acetyl cysteine 3 g per day to increase sperm concentration and sperm motility. Lot of controversy exists regarding long term use of antioxidants. Recent clinical trials have shown that antioxidants do not appear to improve semen para metres or DNA fragmentation among men with male factor infertility. Therefore, limited and judicious use of these drugs is recommended in male infertility and if no improvement is seen in semen parameters in 3 to 4 months or a pregnancy does not occur within 6 months, one must resort to methods of ART to assist in conception.

   To conclude, it is important to remember that there is limited role of medical management in male infertility. What a gynaecologist needs to know is to be able to recognise a sub-normal semen report and to know with certainty when to refer the patient further to an ART clinic or andrologist. However, there are conditions causing subfertility in men which can be managed medically and should be treated before referring the patient to a specialist. Nevertheless, there are a few more conditions like male accessory gland infections (MAGI) and hypo-gonadotropic hypogonadism in men which can be treated success fully by medical management but require either a good local genital examination or hormonal and genetic workup, respectively. These patients need to be referred further without wasting time so that they get the correct treatment and their families can be completed within a stipulated time frame.

OVULATION INDUCTION-NUTS AND BOLTS

Date: 26 May, 2020



Name of the activity :Vibrate
Speaker: Dr Nalini Kaul Mahajan
Key points

1. Disorders of anovulation account for about 20-30% of infertility. Ovulation induction(OI) with or without IUI is performed as a first line treatment in anovulatory, unexplained and mild male infertility.
2. Before initiating OI, it is important to evaluate the underlying cause of anovulation and to treat underlying medical conditions, as applicable. It is also essential to do a semen analysis and tubal patency test before starting treatment.
3. An FSH threshold level is required for follicular recruitment and growth.
4. FSH window - the time for which the FSH level remains at the threshold level. It regulates number of follicles recruited. FSH window needs to be narrow for monofolliculr development.
5. LH is essential for producing the androgen substrate in the early follicular phase, is involved in follicular growth and DF selection and subsequently an LH surge in mid cycle leads to ovulation and formation of corpus luteum(CL).
6. Oral (CC, Tamoxifen, Letrozole) and injectable drugs (GT) are used.
7. H-P-O axis needs to be functional for use of oral drugs.
8. Hypogonadotropic Hypogonadism. Since the GnRH pulses are absent there is need for exogenous GT. (FSH & LH or GnRH). Dose titration required is required to define FSH threshold and FSH window is narrow for monofollicular development. LH surge has to be initiated with HCG, GnRH agonist will not work. Luteal Support is Important
9. PCOS- Basic issue is an Endocrine imbalance- >A. Oral drugs used as first line followed by combination of oral and GT and GT only as a last resort. Recruitable pool of follicles is increased 6 fold so high risk of hyperstimulation and OHSS. Strict dose titration required with GT to define FSH threshold. Use of ISA helpful. If AMH levels >7ng/ml - > dose OI drugs is required. For LH surge – agonist/HCG can be used.
10. Unexplained Infertility - OI+IUI – 1st line treatment, helpful in patients with Infertility > 2yrs and AMA. OI alone not as effective. Oral and GT can be used.
11. LPS is important where GT are used for stimulation to avoid LP deficiency.
12. Fertility drugs do not appear to sign > risk of invasive ovarian, endometrial, BC or other Cancers.0
13. CC more than 7 cycles (esp >2000mg) in subfertile women is associated with > risk of endometril ca. May be due to inherent PCOS risk.(Cochrane 2017)
14. CC should be restricted to 6 cycles. Malignant melanoma & thyroid cancer risk higher among CC treated women in almost all studies. (Yilmaz et al 2017)

LUTEAL PHASE SUPPORT-CASE FILES

Date: 9 June, 2020

Name of the activity :Vibrate
Speaker: Dr Sonia Malik
Topic: Luteal phase support : Case files
Attendees logged in 582

Take home points:
Luteal phase is an enigmatic part of the menstrual cycle. Luteal phase defect is now a known and recognised entity specially in ART cycles but is also found in natural cycles. Luteal phase support is recognised as an essential treatment for good pregnancy outcomes.
LPS varies with the type of patient and cycle. Variables are :Natural IUI IVF
Stimulated Type of protocol Type of trigger Fresh and frozen transfer Each has to be supported on its own merits. Progesterone is the most important molecule for support Route of administration is variable with no difference in outcome. Estrogen and HCG can be used in some types of cycles. Case files were discussed.

ENDOSCOPY IN INFERTILITY

Date: 23 June, 2020

Name of the activity :Vibrate
Speaker: Dr Kuldeep Jain
Topic: Endoscopy in Infertility

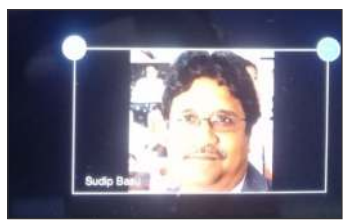
IFS ACTIVITIES 2020

IFS CHAPTER ACTIVITY- TAMIL NADU

- Date: May 22, Friday
- Name of Chapter: IFS Tamil Nadu Chapter
- Chapter Secretary: Dr Rajapriya Ayyappan
- Faculty Was From IFS Tamil Nadu
- Patrons And Committee Members
- 1 Icog Credit Point Was Also Arranged
- Sponsored by- Ferring
- Attended By Over 180 Doctors
- Interactive Discussion On Kickstarting Infertility Practice With Covid

IFS CHAPTER ACTIVITY- WEST BENGAL

- Date : 05-June-2020
- Name of Chapter : IFS West Bengal
- Chapter Secretary: Dr MC Dass
- Sponsored by : Walter Bushnell
- Topic: Panel discussion on restarting fertility treatment in post COVID-19 era in the light of recent guideline issued by IFS.
- Guest Speaker : Local Members



- Total Participants : 1200

We had organised a webinar on 5th June,2020. The topic was panel discussion on restarting fertility treatment in post COVID-19 era in the light of recent guideline issued by IFS, with additional recommendations, if any, based on local circumstances.

The panellists were chosen from local members

The organisers used zoom platform and Facebook which generated viewership of 1200 attendees (data provided by technical team).

IFS CHAPTER ACTIVITY- TELANGANA CHAPTER

- Date : 13th June, 2020
- Name of Chapter: IFS Telangana Chapter
- Chapter Secretary: Dr. Roya Rozati
- Topic: Panel Discussion on "How to Overcome Hurdles & Get the Best Results in IUI in Current Scenario"

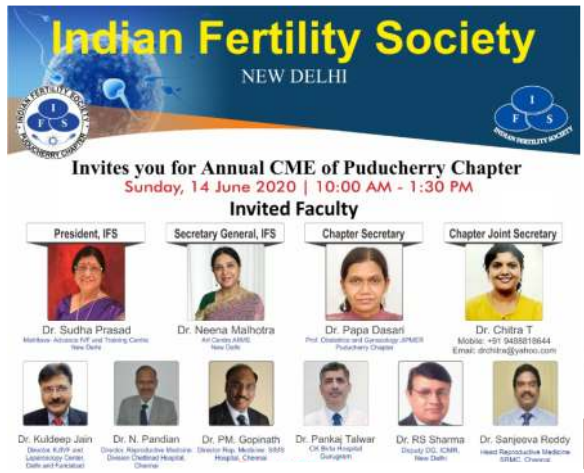
- Moderatores: Dr. K.D. Nayar and Dr. Neena Malhotra
- Panelist: Dr Srilatha Gorthi
  Dr. Swetha Thumula, Dr Krishna Leela
  Dr Swetha Agarwal, Dr.Charulatha Chatterjee
  Dr. Chandana Lakkireddy
  Dr. Krishna Chaitany, Dr. Gaurav Kant
- Total Participants : 124

Indian Fertility society (IFS) Telangana chapter was established in Hyderabad in 2018. Telangana chapter was headed by Dr. Roya Rozati. Webinar was conducted on 13th Jun, 2020 on "How to Overcome Hurdles & Get the Best Results in IUI in Current Scenario"at 18:00 hour to 19:30 hour. Webinar was started by welcome address given Dr. Roya Rozati and presidential address was given by IFS president Dr. Sudha Prasad. Dr. Roya Rozati welcomed guest of honor Dr. Kuldeep Jain followed by his few words about IFS.

Dr. K. D. Nayar and Dr. Neena Malhotra participated in webinar as moderators. Dr. Neena Malhotra explained activities if IFS and why we should join IFS. Dr Srilatha Gorthi, Dr. Swetha Thumula, Dr Krishna Leela, Dr Swetha Agarwal, Dr.Charulatha Chatterjee, Dr. Chandana Lakkireddy, Dr. Krishna Chaitany, Dr. Gaurav Kant were joined as panelist in the webinar. All panelists were introduced by Dr. K. D. Nayar. Total of 34 different questioned were put in front of panelists regarding the how to get best results in IUI in current COVID-19 situation. Questions were put forward in front of panelists by Dr. K. D. Nayar and Dr. Dr. Neena Malhotra. All panelists were actively participated and discussion was very fruitful. Discussion continued for one hour and finally vote of thanks was given by Dr. Roya Rozati.

IFS CHAPTER ACTIVITY- PUDUCHERRY CHAPTER

- **Date : 14-June-2020**
- **Name of Chapter: IFS Puducherry Chapter**
- **Chapter Secretary : Dr Papa Dasari**
- **Sponsored by: Abbott**



IFS CHAPTER ACTIVITY- HARYANA CHAPTER

- **Date : 21th June 2020**
- **Name of Chapter: IFS Haryana Chapter**
- **Chapter Secretary : Dr. Neeru Thakral**
- **Sponsored by: Eris Life Science**
- **Topic: ART Covid Guidelines Practical Issues & Solutions**
- **Guest Speaker : Dr. Sudha Prasad, Dr. Neena Malhotra, Dr. K.D. Nayar, Dr. Kuldeep Jain, Dr. Sanjay Shukla, Dr. Pankaj Talwar, Dr. Manish Machave, Dr. Renu Mishra, Dr. Usha Shekhawat, Dr. Kundan Ingale, Dr. Prasan Vij.**
- **Total Participants : 192**
- Haryana chapter of IFS organised successful webinar on 21 st June under aegis of IFS. Total 192 participants logged in for this webinar . Practical issues related to latest ART COVID GUIDELINES were discussed and resolved by our expert panelist Dr Sudha Prasad(President- IFS) , Dr Neena Malhotra (Secretary IFS) , Dr K.D Nayar (President Elect IFS) and Dr Sanjay Shukla (Secretacy - Accademy of Clinical Embryologist), Dr. Manish Machave (Chairperson Medico Legal & Athical Ethical Committee FOGSI). The panel moderated by Dr Neeru Thakral (chapter secretory) and Dr Shalu Gupta covered the guidelines in detail and was thoroughly enjoyed by all viewer. Second interactive Panel discussion on clinical dilemma in ovulation induction- case scenario was excellent Moderated by Dr Kuldeep Jain (Past President IFS) with esteem panelist Dr Pankaj Talwar (Vice President IFS), Dr Renu Mishra , Dr. Usha Shekhawat (HOD Reproductive Medicine Mgumst-Jaipur), Dr. Kundan Ingale (Pune) ,Dr Ritu Jain, Dr.Prasan Vij (HOD Reproductive Medicine St.Stephen Hospital) and Dr Sonu Balhara . Dr Sonia Malik (Past President IFS) also joined the webinar and gave practical tips on covid ART related queries It was an honour to have all stalwarts under one roof imparting the pearls of knowledge and wisdom and sharing the knowledge. Everyone enjoyed both panel and interactive question answar setion. One ICOG credit point granted for our webinar. Thanks all participants for making it successful. Long live IFS.

Screen Shots of webinar :

IFS CHAPTER ACTIVITY- MP CHAPTER

- **Date : 27th June 2020**
- **Name of Chapter: IFS MP Chapter**
- **Chapter Secretary : Dr Yatindra Singh Verma**
- **Topic: Panel Discussion on Thin Endometrium**

IFS ACTIVITIES 2020

IFS SIG ACTIVITY- ANDROLOGY

- **Name of Activity: Male Infertility**
- **Date : 9th May, 2020**
- **Name of SIG: Andrology**
- **SIG Convenor : Dr. M Venugopal**
- **SIG Co-convener: Dr Gaurav Kant**

The first webinar of IFS ANDROLOGY SIG was held on Saturday May 9, 2020 between 4 to 6 pm.

The meeting was chaired by Dr Sudha Prasad President IFS and Dr Neena Malhotra, Secretary IFS.

The keynote lecture was delivered by Dr Kuldeep Jain on MALE INFERTILITY WHAT WORKS AND WHAT DOES NOT.
The lecture covered in details practical and useful aspects of male infertility and was full of crisp take home messages.

The keynote lecture was followed by a panel discussion on CASE SCENARIOS IN MALE INFERTILITY. The panel was moderated by Dr Venugopal. Eminent panelists included Dr P.M.Gopinath ,Dr Sanjay Makwana,Dr Himanshu Bavishi,Dr Swatantra Rao and Dr K D Nayar. The panel discussion was very interactive.

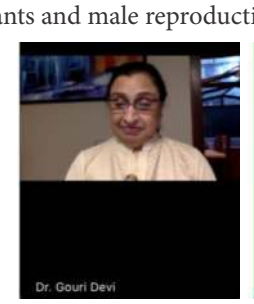
380 delegates from across India logged into this webinar which extended well beyond the two hours allotted.All audience queries were patiently dealt with by the experts.

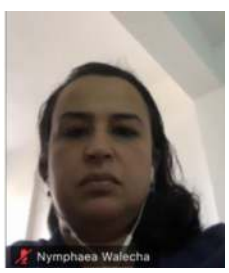
Dr M. Venugopal Dr Gaurav Kant

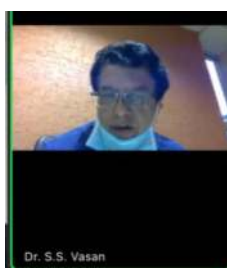
Environment and Fertility

- **Name of Activity: IFS SIG Activity**
- **Date : 5th June, 2020**
- **Name of SIG: Environment and Infertility**
- **SIG Convenor : Dr. Gouri Devi SIG Co-convenor: Dr. Nymphea Walecha**
- **Speakers : Dr. Firuza Parikh ,Dr. S.S.Vasan**
- **1 ICOG Points**

The webinar began with an overview on environment and fertility by Dr.M.Gouri Devi.It was followed by talk on "The effect of Endocrine Disrupting Chemicals (EDCs) on female reproductive health (Indian data on Bisphenol and phalates) by Dr Firuza R.Parikh. She discussed the detrimental effects of EDCs like Bisphenol A, Phalates (Plasticizers), pesticides and industrial pollutants on developing reproductive organs .She also shared outcomes of EARTH and LIFE studies on effect of environment on reproductive health.
The event concluded with presentation on "Environment Toxicants and male reproduction" by Dr.S.S.Vasan.In the end Dr Firuza Parikh suggested a research study on increased incidence of premature ovarian failure, fibroids and adenomyosis and its direct reaction to environmental changes.
It was attended by 118 delegates.
The event was live on you tube and is available for watching
https://youtu.be/jM5W9vh-0Q

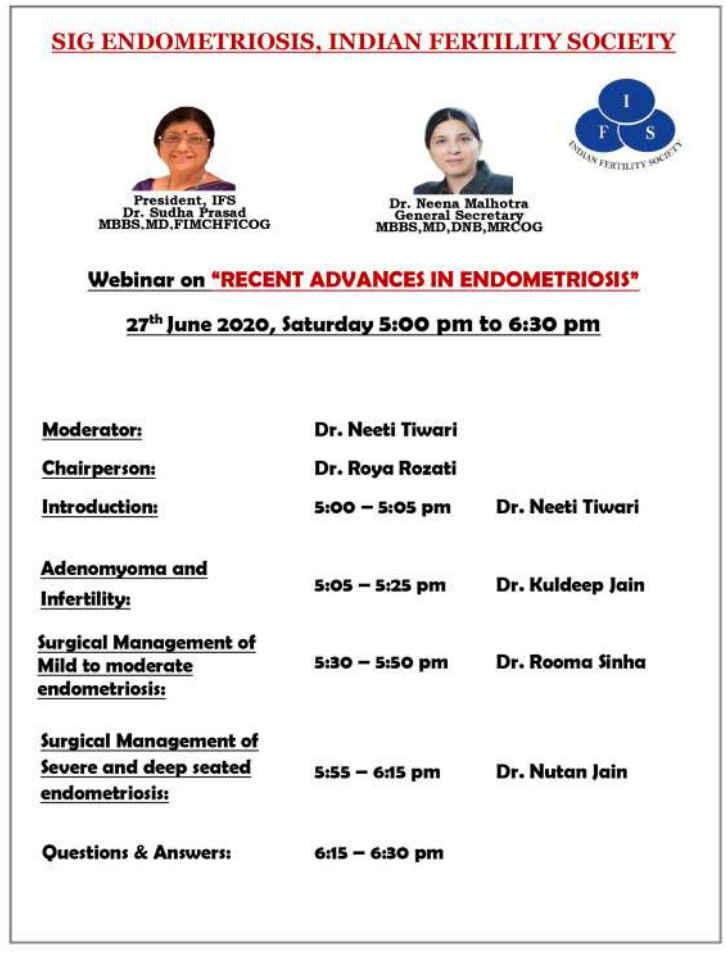






IFS SIG Endometriosis

- Name of Activity: IFS SIG Activity
- Date : 27th June, 2020
- Name of SIG : IFS SIG Endometriosis
- SIG Convenor Name : Dr Roya Rozati
- SIG Co-convener : Dr Neeti Tiwari
- Topic: Recent Advances in Endometriosis



IFS SIG ACTIVITY
Early Pregnancy Considerations

- Name of Activity: IFS SIG Activity
- Date : 28th June, 2020
- Name of SIG : Early Pregnancy Considerations
- SIG Convenor Name : Dr Sonia Malik
- SIG Co -convener: Dr K Aparna Sharma
- Sponsored by: Bayer Zydus
- Topic: Blended Panel Discussion on
- "Early Pregnancy Considerations After Assisted Conception"
- Moderatores: Dr. Sonia Malik and Dr. K Aparna Sharma
- Panelist: Dr. Ashok Khurana, Dr. Bharati Dhorepatil, Dr. Kuldeep Jain and Dr. Neena Malhotra

IFS ACTIVITIES 2020

IFS WEBINAR

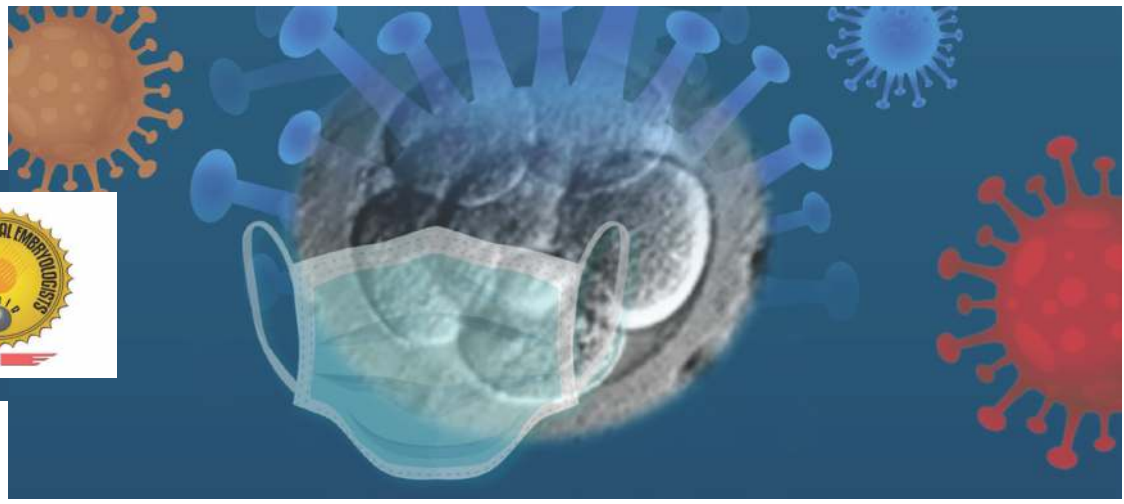
Webinar on Air Quality in the ART Clinic

On 20th June

Speakers : Dr. David Mortimer
Moderator : Dr Prabhakar Singh

The webinar discussed on different parameters related to Safe and Effective Operation of an ART centre's.

JOINT IFS-ISAR-ACE RECOMMENDATIONS ON RESUMING/OPENING UP ART SERVICES



For Details Visit
www.indianfertilitysociety.org

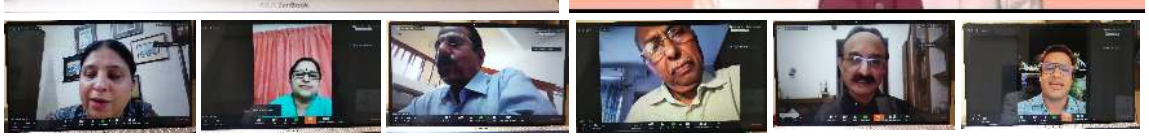
IFS ACTIVITIES 2020

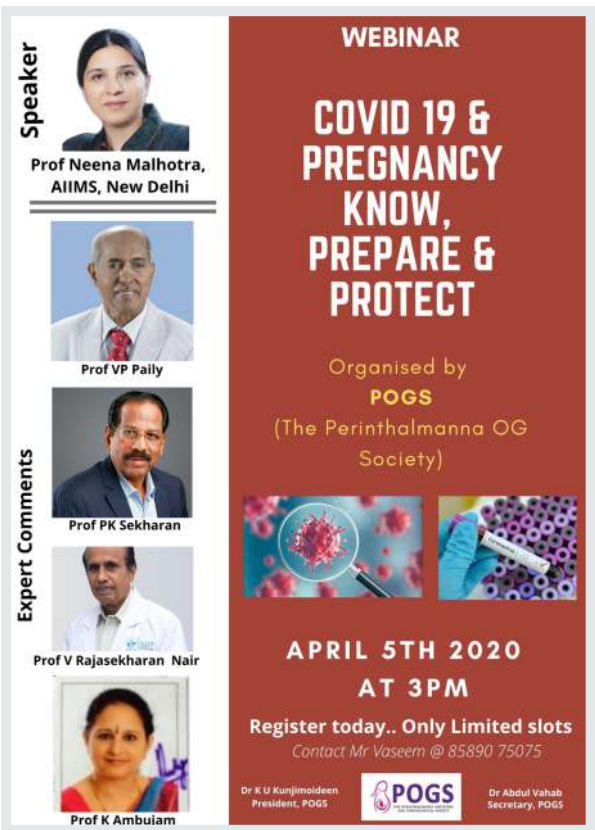
IFS WEBINAR- SOUTH ZONE ACTIVITY

Webinar on COVID 19 & Pregnancy - Report

Perinthalmanna OG Society organized a webinar in association with **Indian Fertility Society South Zone** on 'COVID 19 & Pregnancy – Know, Prepare and Protect' on 5th April 2020. This was the first ever webinar on COVID 19 and Pregnancy organized by any organization. Professor Neena Malhotra, the Professor at AIIMS New Delhi and Hon Secretary General of IFS delivered the lecture and it was massively appreciated by 956 delegates attending from across India.

Prof VP Paily (Thrissur), Prof PK Sekharan (Calicut),
Prof V rajasekharan Nair (Thiruvananthapuram)
and Prof Ambujam(Thrissur) have participated as experts.
Dr K U Kunjimoideen and Dr M Venugopal moderated the session.

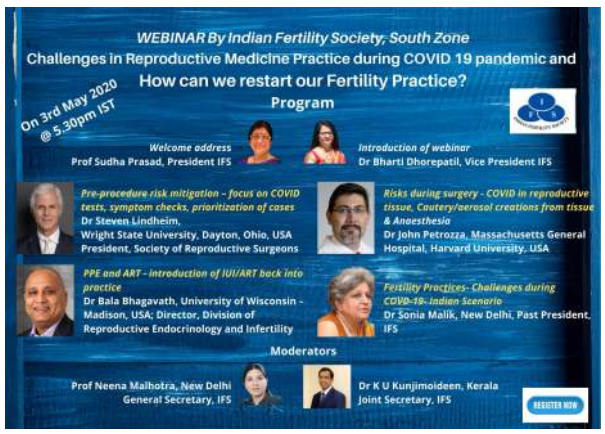




IFS WEBINAR- SOUTH ZONE ACTIVITY

International Webinar on Current scenario of COVID-19 Pandemic and how to restart Fertility Practice 3rd May, 2020

The IFS south zone webinar conducted on current challenges being faced by Reproductive Medicine practice in current scenario of COVID-19 pandemic and how to restart fertility practice now onwards. We had 3 senior faculty from united states of America and one from India.
Dr Steven Lindheim from Wright State University, Ohio, USA, who is also the President, Society of Reproductive Surgeons and also a member of ASRM task force, Dr John Petrozza
From Massachusetts General Hospital, Harvard University where he is the Director, Division of Reproductive Endocrinology and Infertility and Vice President of Society of Reproductive Surgeons, Dr Bala Bhagavath from University of Wisconsin – Madison, where he is Director, Division of Reproductive



Endocrinology and Infertility, Chief Robotic Surgeon and ASRM board member and Dr Sonia Malik, who is a past President of IFS. Dr Sudha Prasad, the President of IFS inaugurated the webinar and Dr Bharti Dhorepatil, Vice President of IFS has formally introduced the faculty. Dr Neena Malhotra, Hon Secretary General of IFS and Dr K U Kunjimoideen, the Joint secretary of IFS have moderated the scientific session. There were 1035 attendees with 239 from abroad and 456 have asked queries. Here is the video clip of the same for those who couldn't log in.

JOURNAL CLUB

1st ISAR-ACE-IFS, JOINT ACTIVITY

Date: 24th April, 2020
Presented By: Dr Krishna Chaitanya Mantravadi
Moderator: Dr vinay Mangoli

Topic: "ESHRE Special Interest Group of Embryology and Alpha Scientists in Reproductive Medicine, The Vienna consensus: report of an expert meeting on the development of ART laboratory performance indicators,

Reproductive Bio Medicine Online (2017), doi: 10.1016/j.rbmo.2017.06.015."
ABSTRACT
Total Quality Management (TQMS) in an In-Vitro fertilization (IVF) lab is a very critical element and a vicious circle. TQMS starts with making a standard operating protocols (SOP) for the lab. Then it involves doing the process as mentioned in the SOP and documenting the performance as required. At fixed intervals internal and external audit of the documented data is essential. Audit data should be benchmarked against Key Performance Indicators (KPIs). If there is any deviation from the KPIs, it calls for troubleshooting or if performance is matching the KPIs then we continue to perform as per the SOPs. For a very long time there was a need for universal KPIs
which would bring about uniformity in Assisted Reproductive Technology (ART) practice. European Society for Human Reproduction and Embryology (ESHRE) and ALPHA Scientists in Reproductive Medicine brought along the best scientists in the field of ART and had a meeting in 2016 at Vienna, Austria to propose a universally acceptable KPIs for ART practice. This review article has proposed KPIs for the IVF lab which would guide ART programs worldwide successfully implement TQMS in their labs. Now IVF labs globally can refer to this document to benchmark their audit data and perform troubleshooting if necessary. As per this consensus statement there is a minimal performance, competency value & a desired performance, Benchmark value. This consensus statement is an important mile stone in the history of ART to ensure safety and success in ART programs globally. Recommendations form this consensus is a general guide for laboratories, however its recommended based on the information presented here, each laboratory should develop its own set of KPIs founded on laboratory organization and processes, and develop a systematic, transparent, and consistent approach to data collection and analysis and calculation of KPIs.

2nd ISAR-ACE-IFS, JOINT ACTIVITY

Date- 1st May, 2020
Presented By: Dr Rajvi Mehta Moderator: Dr Kuldeep Singh

Topic- Striking a balance between innovations and safety concerns in ART.

This paper [Striking a balance between innovation and safety concerns in art [published in Human reproduction Open] starts on the premise that ART have and are being introduced without systematic preclinical safety and effectiveness studies or the follow up of children born through ART or its variants. For a robust safety study, we need to monitor babies till adulthood which is extremely difficult and if we were to wait till the outcomes of this study come out – we would be depriving millions of the technology. Imagine if were to wait to follow-up the first batch of ICSI babies – we would have deprived millions with compromised semen to become fathers. So, we need to strike a balance between introduction of innovations and safety concerns weighing potential risks and advantage.
The discussions focusses on ICSI, use of non-ejaculated sperm, pre-implantation genetic testing and mitochondrial replacement therapy. Studies show that ICSI is associated with a significantly high risk of very preterm deliveries; lower mean birth weight and increased risk of rare imprinting disorders in comparison to spontaneous conceptions. There is no data showing it to be more effective than conventional IVF for conditions other than male infertility. Thus, there is no merit in using ICSI for all as the potential risk is greater than potential advantage.
There were lot of theoretical concerns on the use of non-ejaculated sperms in the initial days. Leaning towards extreme caution, there was a national moratorium against its use in Netherlands; after data from animal studies and other countries, the moratorium was lifted in 2012 for epididymal sperms and 2014 for testicular sperms. In this case study of extreme caution, many patients with male factor infertility were deprived of treatment.
As far as PGT-A was concerned, there were some concerns about the procedure itself, the removal of cells for biopsy and extended culture. Studies show that PGT-A is fairly safe. However, when we study the effectiveness of PGT-A, the evidence is still lacking and the treatment rationale is still under discussion. Follow-up studies on the health of the children born after PGT in combination with trophectoderm biopsy are still very limited. The paper concludes that PGT-A should be used as an add-on to IVF only in couples with advanced maternal age, repeated miscarriages and repeated pregnancy loss and not for other indications as there is limited evidence of its efficacy.

A lot of pre-clinical research that has been done on mitochondrial replacement therapy in animal studies especially in the UK and its use has been allowed for mitochondrial diseases. However, there have been reports of mitochondrial spindle transfer in countries where there are not strict guidelines for cases of female infertility as a means of "rejuvenating the eggs of older women". Mitochondrial replacement therapy for fertility problems may be less risky but there are no proven benefits or evidence for its effectiveness.
The presentation concluded that we should not rush into a technology just because it is available but we need to consider the outcome about a healthy child. We need to strike a balance and use it for indications and avoid over treatment.
Link for the talk - https://www.youtube.com/watch?v=wMyt3JXGL1g

3rd ISAR-ACE-IFS, JOINT ACTIVITY

Date – 15th May, 2020
Presented By – Dr Priya Kannan
Topic – Are cleavage anomalies, multinucleation, or specific cell cycle kinetics observed with time-lapse imaging predictive of embryo developmental capacity or ploidy

Nina Desai, Jeffrey M. Goldberg, M.D., Cynthia Austin, M.D. , Tommaso Falcone, M.D.
April 2018 Volume 109, Issue 4, Pages 665–674
Name of the chapter – Tamil Nadu
How many People attended – 190
Key points –
As per this publication,

1) Early cell cycle kinetics, while predictive of embryo developmental capacity to blastocyst, do not correlate to embryo ploidy
2) Late kinetic parameters tSB, tEB, and tEB-tSB appear to be associated with likelihood of euploidy (even after adjustment for maternal age).
3) Embryo cleavage anomalies as well as MU alone were not directly correlated to likelihood of bl
4) Deselecting for embryos with two or more dysmorphisms significantly increases the odds of euploidy and potentially successful implantation.

4th ISAR-ACE-IFS, JOINT ACTIVITY

Date: 29th May, 2020
Presented by: Dr Varsha Samson Roy
Moderator: Dr Gaurav Majumdar
Topic- Day 5 versus Day 6 blastocyst transfers: a systemic review and meta-analysis of clinical outcomes.
The last decade has seen a significant change in the embryo transfer policies with blastocyst stage transfer taking precedence over the cleavage stage.
The article by Mathilde Bourdon et al, in Hum Reprod vol 34, No. 10; 2019, addresses the issue of day (D5 vs D6) of blastocyst transfer & its impact on the clinical outcomes.
The conduct and reporting of this review was guided by PRISMA. All the 29 studies included (2005-2018) were based on D5/D6 transfers & included fresh &/or FET. The primary outcome studied was CPR & the secondary outcomes studied were IR, OPR, LBR & miscarriage rate(MR).
Apart from the overall outcome (Fresh + FET) the FET group was sub grouped according to the method of cryopreservation (vitrification & slow freeze).
In the primary outcome for CPR a total of 12,837 transfers (D5 -8110 & D6 -4727) were analyzed.
The overall CPR (fresh and /or FET) was significantly higher for D5 compared to D6 transfers.
Similar was the finding when the transfers were sub grouped into fresh, vitrified & warmed, slow frozen & thawed.
Results of the secondary outcomes showed that the overall IR, OPR & LBR were significantly higher for D5 transfers & also in the fresh & vitrified FET group but no significant difference was noted in the slow freeze thaw group.
An association was detected between risk of miscarriage & day of blastocyst expansion - a higher risk was identified with D6 compared to D5 ET- in overall & fresh only & FET-vitrified ET cycles.
A sensitivity analysis of the embryo quality revealed an overall significantly higher CPR & OPR with D5 transfers whatever the embryo quality. Only 2 studies which looked at D5 Vs D6 Euploid transfers found no difference in the CPR, OPR & LBR.
No significant difference in the any of the primary or secondary outcomes were noted in the slow freeze – thaw transfer group.
Lack of power in the slow freeze group is a limitation of this review, however most clinics today have moved away from slow freeze & cryopreserve their embryos by vitrification method.
Another Limitation is that this review is based on observational studies, some of which did not adjust fo excluded.
This review is the first that has that has looked at effects of delayed blastocyst development (D5 vs D6) on the outcome of fresh & frozen ET.
In clinical practice, when both D5 & D6 are available, it appears reasonable to transfer first D5. For those with only D6 embryos the chances of pregnancy may be lower but still persist & D6 should be

5th ISAR-ACE-IFS, JOINT ACTIVITY

Date: 12th June, 2020
Presented by: Dr. Sujatha Ramakrishnan, Senior Embryologist, Chennai
Moderator- Dr. Sankalp Singh, Director, Reproductive Medicine Unit

Topic- Is there an association between oocyte number and embryo quality?
A Systematic review and meta-analysis.

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- Cryobiology
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