INDIAN FERTILITY SOCIETY

IFS CONVERSATIONS

Volume 8 : July, 2019

INTERESTING CASES & MANAGEMENT IN INFERTILITY

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MESSAGE FROM THE PRESIDENT DESK

DR GOURI DEVI
President - IFS

Dear Friends,
It is always a pleasure to communicate with all members of IFS and we always go out of the way to be with you all. This year we have done many focused meetings. Environment and ART, Setting up of ART lab and clinic, RiskfreeART,Recent Advances in ART are some of them held in different cities of India. We have been successful in spreading awareness of Infertility, its causes and available treatment modalities.

It has been our endeavor to spread knowledge among doctors and also to update them on the latest available techniques and guidelines. We always kept ethical and legal issues on the forefront.

Our prestigious Annual conference this year is From 6-8th december2019 at Leela Ambience, Gurgaon. We have 9 work shops lined up. The theme is "Beyond tomorrow". We have a galaxy of International and National speakers. I request all the members to actively participate.

This issue of IFS Conversations deal with interesting topics - Hypogonadotropic hypogonadism, Critical OHSS, Empty follicle syndrome. The writers have taken a lot of effort to put these together. Hope you all will gain from this news bulletin.

With best wishes,

Dr M. Gouri Devi

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MESSAGE FROM THE SECRETARY'S DESK

DR (PROF) PANKAJ TALWAR
Secretary General - IFS

Dear Friends,

It gives me immense pleasure to introduce to all IFS members the next edition of "IFS Conversation".

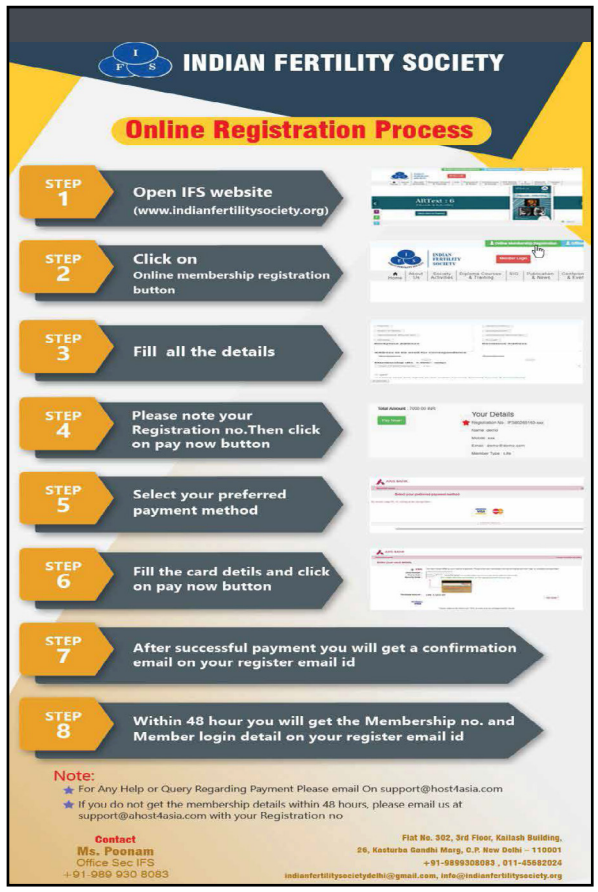
I would like to congratulate the dynamic team of Dr shweta Mittal and Dr surveen Gumman who have spent there valuable time in compiling this bulletin, the authors and contributors for their efforts in providing in depth information and keeping us all updated with recent advances in the field Opinions on the controversies in ethical and legal issues, contributed by experts across the country are deeply appreciated.

IFS has been doing excellent work by focussing on academic activities all over the country, helping young faculty to learn from experienced senior members. Indian Fertility Society (IFS) has progressed over the few years with nearly 2600 members and 26chapters. It is an internationally affiliated organization engaged in training and educating clinicians and embryologists by organizing CME, workshops andseminars.

Through thisedition of newsletter, the Editorial team has tried to answer all the queries related to some burning issues in ART by providing in depth information and keeping us all updated with the recent advances in the field contributed by experts across the country. We are discussing daliy challenges as Empty follicle syndrome, OHSS, Hypogonadism etc. in this bulletin.

I will also take this opportunity to welcome you all to the 15th Annual National IFS Conference, FERTIVISION 2019 at Gurugram, where all the clinicians and embryologists not only learn but also share their experience and present their scientific work.

Dr (Prof) Pankaj Talwar



MESSAGE FROM THE EDITOR'S DESK

DR SURVEEN GHUMMAN
Editor - IFS

DR SHWETA GUPTA
Jt. Editor - IFS

Dear Friends,

Greeting from team IFS!

We have come out with the next issue of IFS conversations. After a successful fertivision conference in Kerala, attended in large numbers by national and international faculty and delegates. The conference had extensive discussions on recent progress in the field of ART and was a platform for all clinicians and stalwarts to meet for deliberations.

In this issue we have brought forward clinical dilemmas and solutions as case based observations. We are discussing interesting cases in Infertility - A case on poor responder and its management, Ovarian Hyperstimulation Syndrome although now rare is still the largest scare for an ART specialist, PCOS - a case discussion on management dilemmas Other interesting cases of endometriosis and hypogonadotropichypogonadism which have a specific management.

In 2019 more chapters have been added and IFS continues to grow. On the academic front multiple academic meets on research, quality and clinical issues have been organized all over the country reaching even remote areas. This issue brings forth these activities done by chapters, and special interest groups pan India.

Hope you enjoy reading our updates of 2019 in IFS Conversations!

Dr Surveen Ghumman

Dr Shweta Mittal Gupta

INDIAN FERTILITY SOCIETY INITIATIVES

INVITED ARTICLES

Non-Classical Congenital Adrenal Hyperplasia (NCCAH) – A Diagnostic Dilemma

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Introduction

Congenital adrenal hyperplasia is a group of autosomal recessive disorder caused by 21- hydroxylase deficiency. Based on haplotype association studies, nonclassic forms of CAH were estimated to have a prevalence of 1:500 to 1:1000 in the general white population but up to 1:50 to 1:100 among populations with high rates of consanguineous marriages. More recent CYP21A2 genotype analysis indicates that NCCAH has an overall frequency of;1:200 (95% confidence level, 1:100 to 1:280) in the US population.[1]

A cardinal feature of classic or severe virilizing CAH in new born females is abnormal development of the external genitalia with variable extent of virilization. The degree of 21- hydroxylase deficiency affects the severity of clinical spectrum. It can be either simply virilizingor salt wasting type in classical CAH (1 in 10,000 to 1 in 20,000) or manifest variable signs of androgen excess at any phase of postnatal development in NCCAH(1 in 1000). Those with NCCAH have normal external genitalia and present late during childhood or early adolescent with precocious puberty or as a young adult with other signs of hyperandrogenemiasuch as acne, hirsutism, and menstruatal irregularities along with infertility very much like PCOS.About 40% of cases withNCCAH have polycystic ovaries; insulin resistance which is a feature ofPCOS might be seen in NCCAH. Both have a strong familial preponderance.Here we are presenting a caseof an infertile womanwho presented with features of hyperandrogenism and irregular cycles and was being managed as PCOS but on investigations turned out to be a case of non-classical congenital adrenal hyperplasia hence was a diagnostic dilemma.[2]

Case report

A 30 year old nulliparous womanvisited the Gynaecology OPD seeking treatment for infertility, having being married for 7 years with history of secondary amenorrhea since 1 year. She had been seeking treatment at various infertility clinicswhere she was diagnosed as a case of polycystic ovarian syndrome with hypothyroidism and had received 3 cycles of Ovulationinduction and according to the patient dominant follicle was formed and ruptured but poor endometrial growth was noted in all three cycles.

Her menstural history revealed that initially the cycles were prolonged after a period of 35-40 days followed by oligomenorrhea. She used to get her periods after withdrawal with Oral Contraceptive pills which werefollowed by secondary amenorrhea.

She also gives history of excessive thick hair growth over face,chest, abdomen thighs and legs. Her hair growth was of such a concern to her that she had to get laser treatment to remove them. Her secondary sexual characterswere well developed and there was no history of early pubarche or delayed menarche.There was no history of tuberculosis or history of contact with a known case of tuberculosis.

On examination she had an average built with BMI of 27, Ferriman Gallwey score of 16, noacne, pigmentation or stria.Secondary sexual characters were well developed with sexual maturity rating (SMR) was stage 5. On pelvic examination no abnormality was noted, external genitalia was normal ,no signs of clitoromegaly seen her clitoral index was 35mm

Herbaseline ultrasound showed a hypoplastic uteruswith thin ET -2.5mm and Antral follicle count of 3 in right and 4 in left ovary and no other pathology noted.

On detail investigation tuberculosis was ruled. Endometrial aspiration report of histopathology showed few endometrial glands and the sample was sterile for AFB stain and culture. Hormonal profile revealed Serum FSH 1.4 IU/ml, LH 3.1 IU/ml,serum prolactin 9.4 ng/ml,serum estradiol 52.3IU/ml, serum AMH 8.5 ng/ml, serum TSH1.6 microIU/ml(controlled on tab Eltroxin 75mcg)

In view of hyperandrogenemiafurther investigations were done.

17alphaOHP	↑ 18.0ng/ml	0.2-4.5ng/ml
Free testosterone	↑ 20pg/ml	0-3pg/ml
DHEAS	↑ 5.0mcg/ml	0.4-2.2 mcg/ml
S.CORTISOL	70ng/ml	50-230ng/ml

Endocrinology opinion was taken for increased DHEAs, 17alpha -OHP and Serum free testosterone. MRI to image the adrenals and ovaries was done to find the source of androgens.

MRI- Showed a hypoplastic uteruswith narrow endometrial strip;rest of the pelvis was normal and no other abnormality was detected. Ovaries and adrenals were normal.

Further evaluation in view of hyperandrogenemia was done to rule out Cushing syndrome byovernight dexamethasone suppression test and serum cortisol level at 9am was done which were 0.81mcg /dl (in normal range).17 alpha hydroxyprogesteronewas repeated,it wasraised >36.0 ng /ml(0.25-2.91ng/ml)confirming the diagnosis of NCCAH.

In our case the infertile women has been counselled about the risk associated to mother and fetus if she conceives with NCCAH. she has been put on estradiol therapy in view of poor endometrial growth and planned for ovulation induction once the Endometrium is favourable.

Discussion

Symptomatic androgen excess in women of reproductive age is a common presentation to the general Gynecology clinic as well asin adolescent and infertility clinic The physical effects of hyperandrogenism are distressing for many patients but nonetheless a detailed history and thorough clinical examination are essential.

Hirsutism that is sudden in onset, moderate orsevere, rapid progressive or associated with signs and symptoms of virilizationwarrants further lab investigations to rule out other causes of hyperandrogenism as congenital adrenal hyperplasia, Cushing's syndrome, androgen secreting tumours apart from PCOS which is usually associated with chronic anovulation and excess ovarian androgen production.

The serum total testosterone concentration provides the best overall measure of androgen production and is the only hormone that need be measured in most women with hirsutism who merit evaluation. Nearly all women with PCOS have a testosterone level less than 150 ng/dL (1500 pg/mL), as do all women with idiopathic hirsutism, by definition. The suggested threshold value has very high sensitivity and negative predictive value, indicating that it diagnoses virtually all women with tumours causing hirsutism and can effectively exclude the diagnosis.

The diagnosis of suspected case of CAH needs to be evaluated with serum 17 hydroxyprogesterone level to be measured in follicular phase of cycle in morning before 8.00 am and if the levels are >800ng/dl diagnosis of NCCAH is confirmed. In cases where the value of 17-OHP is 200-800ng/dl ACTH stimulation test is done. samples are drawn at time 0 and 60 min later after injecting 0.25mg ACTH Intravenous and the 17-OHP levels are measured, a value of >1500 ng/dl is diagnostic. Value of 17 – OHP <200 ng/dl rules out 21 hydroxylase deficiency. Since in our case values were3600ng/dl ACTH stimulation test was not required for confirming the diagnosis.

Non-classic congenital adrenal hyperplasia (NCCAH) is a condition that usually develops around the age of puberty and can impact both boys and girls. NCCAH is an inherited condition where deficiency of a specific enzyme, 21-hydroxylase that converts the hormone progesterone into cortisol. NCCAH is a cause of

hyperandrogenemia in less than 2% patients. The mild subclinical impairment of cortisol synthesis in nonclassic CAH (NCCAH) generally does not lead to Addisonian crises but it leads to hyperandrogenemia and infertility . Testing for nonclassic CAH can be safely reserved for patients with an early onset of hirsutism (pre- or peri – menarchealonset, including those with premature adrenarche), women with a family history of the disorder, and those in high-risk ethnic groups (Hispanic, Mediterranean, Slavic, or Ashkenazi Jewish heritage). Additional evaluation also is indicated for those with hirsutism having onset before puberty or after age 25, rapidly progressive hirsutism, or hirsutism that is accompanied by signs of virilization or hypercortisolism (Cushing syndrome).

Treatment for NCCAH:

In adolescents with irregular menses and acne, symptoms are usually reversed within 3 months of glucocorticoidtreatment, whereas hirsutism remission is more difficult with glucocorticoid monotherapy. As in other androgenic disorders, an oral contraceptive with or without anti- androgens is likely the best approach for treating hirsutism in women with NCCAH. For patients treated in childhood or adolescence, it may be reasonable to consider tapering and discontinuing Glucocorticoid (GC) treatment once near-adult height has been reached.Women with subfertility may benefit from GC treatment to conceive and maintain pregnancy. In study by Moran et al and Bidet et al GC treatment was given to induce fertility in 23% and 42% of cases . Both studies reported elevated miscarriage rates of 25% in those not receiving GC and 6% in those exposed to GC. A third report found no difference in miscarriage rate between GC-treated and untreated women, but the former group had a shorter time to conception.[1]

The infertile women with NCCAH needs to be counselled about the risk associated.Theoretically, and without genotyping, a NCCAH parent has an;1:250 risk of having a child with classic CAH [(0.7 3 0.5) 3 (0.02 3 0.5) = 0.4%]. However, in two retrospective analyses of children born to women with NCCAH, the risk was higher, at 1.5% to 2.5% .To refine the risk, CYP21A2 genotyping is recommended prior to pregnancy planning.

Prenatal diagnosis is available for some forms of congenital adrenal hyperplasia. Diagnosis is made in the first trimester by chorionic villus sampling. Diagnosis in the second trimester is made by measuring hormones such as 17-hydroxyprogesterone in the amniotic fluid. Prenatal treatment has been suggested for women who have previously delivered a child with CAH and are pregnant again via the same partner. The foetus will have a 1:4 chance of having CAH and a 1:2 chance of being female; thus, there is a 1:8 chance that the foetus will be female and have CAH1 , the period during which foetal genitalia may become virilized begins;6 weeks after conception, therefore in women with CAH who become pregnant it is recommended to continue pre-pregnancy doses of Hydrocortisone / prednisolone or fludrocortisone therapy, with dosage adjustments if symptoms and signs of GC insufficiency occur1, or must be started on steroid therapy by 6 to 7 weeks of pregnancy . Because genetic diagnosis by chorionic villous biopsy cannot be performed until 10 to 12 weeks, all pregnancies at risk for CAH would need to be treated with steroids. Clinicians should not use Dexamethasone, or other steroids that are not inactivated by placental 11b-HSD2, to treat pregnant women affected by CAH. There are no data and no widely accepted recommendations for managing GC doses in pregnancy.[1]

References:

1. Speiser PW, Arlt W, Auchus RJ, Baskin LS, Conway G S, Merke D P, White P C . Congenital Adrenal Hyperplasia Due to Steroid 21-Hydroxylase Deficiency: An Endocrine Society Clinical Practice Guideline. The Journal of Clinical Endocrinology & Metabolis.,2018;103(11), 4043-4088. doi:10.1210/jc.2018-01865
2. Jain P, Bhalerao AV, Aggarwal S. Late-onset Congenital Adrenal Hyperplasia or Early-onset Polycystic Ovarian Syndrome: A Clinical Dilemma. Journal of SAFOG with DVD.2017;9(4(Supplement)), 441-443. doi:10.5005/jp-journals-10006-1546
3. Fritz, M. A., &Speroff, L. (2011). Clinical Gynecologic Endocrinology and Infertility (8th ed.). Lippincott Williams & Wilkins.
4. Moran C, Azziz R, Weintrob N, Witchel SF, RohmerV, Dewailly D, Marcondes JAM, Pugeat M, Speiser PW, Pignatelli D, Mendonca BB, BachegaTAS, Escobar-Morreale, HF, Carmina E, Fruzzetti F, KelestimurF. Reproductive outcome of women with 21-hydroxylase-deficient nonclassic adrenal hyperplasia. The Journal of Clinical Endocrinology & Metabolism.2006;91(9),3451–3456.doi: 10.1210/jc.2006-0062
5. Bidet M, Bellanne´-Chantelot C, Galand-Portier MB, Golmard JL, Tardy V, Morel Y, Clauin S, Coussieu C, Boudou P, Mowzowicz I, Bachelot A, Touraine P, Kuttenn F.Fertility in women with nonclassical congenital adrenal hyperplasia due to 21-hydroxylase deficiency.2010;The Journal of Clinical Endocrinology & Metabolism,95(3), 1182–1190.

Enigma of Ovulatory Dysfunction – A case of Hypogonadotropic hypogonadism

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Introduction

World Health Organization (WHO) has classified hypogonadotropic hypogonadism as group1anovulation disorder[1]. Hypogonadotropic hypogonadism are mostly due to idiopathic causes[2]. They are usually characterised by amenorrhoea, hypoestrogenism and low gonadotropins levels. In these women with infertility, induction using higher dose of exogenous gonadotropin for longer duration of stimulation are required to make the inactive ovaries active to achieve good follicular response.

Case Report

Mrs X, 26 year, a case of secondary amenorrhoea came with primary infertility of 4 years for evaluation. She gave history of secondary amenorrhoea of 6 months duration and prior to that she had periods with withdrawal medicines only. In the past she had undergone repeated cycles of ovulation induction. Most of the cycles were cancelled due to non responsiveness. So with a provisional diagnosis of PCO with anovulation and was referred to us for further management. On clinical examination female having eunuchoid habitus with height 155cm, weight 62.4 kg with BMI of 26kg/m2. She was having normal pubic hair and breast development. Clinical examination revealed normal sized uterus. Baseline trans vaginal ultrasound showed a small uterus with right and left ovary measuring 2.9x2x2.3cm and 2.8x2.3x1.9cm. Her hormonal profile include : Serum FSH – 0.9mIU/ml, LH – 0.8mIU/ml, Estradiol – 16pg/ml, AMH – 3.8ng/ml and TSH and prolactin within normal limits. The patient`s husband had sperm concentration of 80million/ml with progressive motility of 70%. We had a provisional diagnosis of secondary hypogonadotropic hypogonadism. She was evaluated to find a cause for secondary hypogonadotropic hypogonadism, but no conclusion was drawn. After counselling about the diagnosis, costs and success of treatment modality, the couples was planned for ovulation induction and IUI. Following withdrawal bleed with OCP, the patient was started on 300IU of hMG(Human Menopausal Gonadotropin) on day 2 of cycle for 12 days stimulation with a total dose of 3600 IU. A single follicle of 20mm developed on the right ovary with endometrial thickness of 9mm. Ovulation trigger with 10,000IU of hCG given. IUI done after 36 hours of trigger. Post IUI luteal phase support was given with oral estradiol tablets and micronized progesterone vaginally. IUI resulted in a singleton clinical pregnancy.

Discussion

Among the different causes for infertility, anovulation accounts for 25% of cases[3]. The different causes for anovulation include PCOS, hyperprolactinemia, thyroid dysfunction, hypogonadotropic hypogonadism etc. From the current case scenario these are the differential diagnosis we kept in mind. Secondary amenorrhoea with low gonadotropin and estradiol level with other normal hormonal profile suggested the diagnosis of secondary hypogonadotropic hypogonadism. From the case it is clear that hypogonadotropic hypogonadic patients respond to high dose of gonadotropin stimulation producing favourable results.

Hypogonadotropic hypogonadism is a cause of anovulation characterised by the absence of normal hypothalamic – pituitary synchronous activity. These group of patients belong to WHO class I ovulatory dysfunction accounting for 10% of total cases of anovulation[4].

In case of hypogonadotropic hypogonadism, the response to stimulation cannot be predicted from the initial hormonal assay value. The AMH has limitations in assessing the ovarian reserve because it only reflects the growing follicular pool that is responsive to gonadotropins. Hence, conditions that cause a permanent or sustained interruption of gonadotropin release may lead toa decrease AMH levels and therefore an underestimation ofthe true ovarian reserve suggesting that AMH may not be a very good predictor of ovarian reserve in patients with hypo hypo patients.

The treatment modalities available to the hypo hypo patients include GnRH supplementation or administering gonadotropins for stimulation. Gonadotropins treatment is the accepted method of ovulation induction in such patients. The optimal results are obtained by using FSH combined with LH [5] which is accomplished by administering HMG or recombinant LH and FSH. The success of ovulation induction has been reported as high as 60-80% with a multiple pregnancy rate of 20-50%[6]. So to avoid multiple pregnancy rates in these patients, they may require a longer duration of stimulation[7].

Ovulation induction in a hypogonadotropic hypogonadic patient is a real challenge to the treating physician . Ovarian reserve assessment is difficult in these set of patients and have to be done carefully. To conclude, high dose of gonadotropins in WHO type I anovulation produces a favourable results. So before recommending straight away ART procedures to these patients, IUI is a fruitable option to the appropriately selected hypo hypo patients. They need proper counselling about the need for high dose, prolonged gonadotropin usage, cost incurred and the chance of success.

Reference

1. WHO- classification of anovulation: background, evidence and problems. International Congress Series.2015; 1279:3-9.
2. Silveira LF, MacColl GS, Bouloux PM. Hypogonadotropic hypogonadism. SeminReprod Med 2002;20:327-38.
3. Hull MG, Glazener CM, Kelly NJ, et al. Population study of causes, treatment, and outcome of infertility. Br Med J (Clin Res Ed) 1985; 291:1693.
4. Aboulghar M, Rizk B. Ovarian Stimulation. 1st ed. Cambridge University Press; 2011. p. 162-8.
5. Burgués S; Spanish Collaborative Group on Female Hypogonadotrophic Hypogonadism. The effectiveness and safety of recombinant human LH to support follicular development induced by recombinant human FSH in WHO group I anovulation: Evidence from a multicentre study in Spain. Hum Reprod 2001;16:2525-32.
6. Allahbadia G. Manual of Ovulation Induction. 1st ed. Rotunda Medical Technologies PVT .LTD; 2001. p. 93-4.
7. Kumbak B, Kahraman S. Women with hypogonadotropic hypogonadism: Cycle characteristics and results of assisted reproductive techniques. Acta Obstet Gynecol Scand 2006;85:1453-7.

Delayed interval delivery (DID) with raised markers of infection and emergency cervical cerclage -A case report and review of literature

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Introduction

With the increasing use of assisted reproductive technology, there is a manifold rise in incidence of multiple gestation. Multi fetal pregnancies are often complicated by spontaneous preterm delivery, thereby placing the neonates at risk for prolonged hospitalization, serious morbidity, and mortality. Typically, all fetuses of a multiple gestation deliver within a short interval; however, in selected cases, the preterm birth of one fetus may not require delivery of the other fetus(es). An extended time interval between births of siblings at a critical gestational age may improve neonatal survival and reduce morbidity from preterm birth. We report a case in which first twin delivered at 22 weeks and second twin was delivered at 31 weeks with favourable outcome in a patient with previous 6 IVF failures .

Case Report

A 41 year old woman married for 7 years underwent sixth IVF (with donor eggs) at our centre with history of abortion at 16 weeks in previous IVF. She had a Dichorionic -Diamniotic twin gestation and progressed successfully. All her routine investigations and obstetric ultrasounds were normal. She underwent Mc donald stich application at 13 weeks considering prior history of midterm abortion and twin pregnancy this time .She came at 22+4 weeks for follow up with ultrasound which revealed severe oligohydramnios of the first fetus. the second twin had normal amniotic fluid index. Leading questions were asked and patient gave history of vaginal discharge for past 10 days. On examination she had leaking PV and closed cervix. Her Total leucocyte count and CRP were high (18000/cmm and 9.4 mg/L respectively). The patient was treated with bed rest and antibiotics(inj ceftriaxone and inj Metrogyl).

On second day of her admission she complained of something coming out per vaginally. On examination fetal parts were felt per vaginum. Patient was taken to the labor room. Her Mc Donald stich was removed and fetusexpelled. Cord was clamped. Patient had no uterine contractions post expulsion of first fetus and was observed for 1 hour. After detailed counselling about the possible benefits and risks , the couple decided to take a chance with delayed delivery of the remaining fetus.

After informed consent decision was taken to legate the umbilical cord of the first twin, as high in the cervix as possible. Cord was clamped and repeat Mc Donald's was applied in aseptic condition, and the placenta was left inside the uterus. Her TLC count and CRP started declining from the next day(12,000/cmm , 5.3 mg/L).

She was kept on same injectable antibiotics for 1 week followed by oral cefixime and metrogyl for 2 more weeks. She was initially monitored every alternate day with TLC along with daily 4 hourly monitoring of temp, pulse ,uterine contractions, tenderness etc. Her ultrasound and colour doppler was done weekly to assess fetalwell being. She remained afebrile throughout hospital course. Two doses of 12 mg of betamethasone were also given intramuscularly at 26 weeks. She had Leaking PV at 31 weeks when her LSCS was done and a healthy though premature female child was born (59 days interval period). Two placentas were delivered, one of which was small, fibrous and calcified, with a narrow necrotic umbilical cord. The post-operative recovery of mother was uneventful. The neonate stayed in the NICU for 28 days and discharged in a healthy condition.

Review of literature

In recent years the approach to the fate of after coming twin has changed. In couples suffering from infertility and attempting ART, desperate attempts to salvage the second twin have been tried recently , in cases of premature delivery of the first twin. To evaluate survival benefit of the second twin from delayed interval delivery compared to the first twin, literature was reviewed.

First case report of delayed interval delivery (DID) was reported by Corson(1) in 1880 in the BMJ in a case with uterine didelphys. Between 1880 and the mid 1950's there were sporadic case reports of similar occurrences of uterine didelphys pregnancies with intervals up to 56 days, occasionally despite attempts to deliver with pitocin. In 1957 Abrams (2) reported a DID in a normal uterus with a delay of 35 days. The first twin was 14oz and died soon after birth. The second twin was 2lbs 4ozs and survived. The mother did well. Drucker et al (3) reported in 1960 a 65 day DID with antibiotics in a normal uterus.

Earlier after the premature delivery of first twin no intervention was done to ,purposefully prolong the duration of delivery of second twin ,not expecting a favourable outcome .Many articles cited that the perinatal mortality rate of a retained second twin was higher than that of a first twin and was related to the period of retention.(4) Even Active intervention by way of operative procedure or induction was done to deliver second twin .

First attempt of purposeful prolongation of gestation was done by Eiecher (5)in 1970 and was successful in prolonging the delivery interval by 72 days after the first birth, with the use of sedatives ,progesterone and tocolytics.

Thomsen, (6)1978, reported a DID with the first mention of the use of a cerclage and antibiotics ,tocolytics and dexamethasone . In 1980's some cases are reported in the literature with Twins and triplets with Intervals of 5-131 days between deliveries. Some using cerclage, most using tocolysis and antibiotics showing 100% first twin death and high mortality of second twin.

The first systematic review of Delayed interval delivery in multifetal pregnancy was done in 1998 by Porreco, Diss Sabin, Heyborne and Lindsay(7). The perinatal mortality of firstborn infants in pregnancies in which a delayed-interval delivery was attempted was 70%, compared with 18% for the fetuses who were retained after the birth of their sibling(s).

In a retrospective study in 2000 (8), with 24 twin pregnancies in whom delayed interval delivery was attempted the mean latency interval was 36 days, with a range of 3 to 123 days. Additionally, patients with previous cerclage(s) had significantly shorter mean latency intervals than patients without previous cerclage(s). Patients with long latency intervals (> or =49 days) had earlier births of the first fetus.

Recent systematic review by Feys et al., shows clear evidence of lower mortality risk of the second twin with DID (9)

A question to be answered was whether circlage should beperformed or not. Arabin et al(10), did not perform it at all in their 17-year study, due to the potential risk that this invasive technique represents to the potentially infected gestational sac.. However, Ariad et al(11). did it systematically to reduce the exposure of the amniotic membranes to the septic environment of the vagina. Fayad et al. [12] only did it when there were changes in the cervix during follow-up. None of these three options have caused a significant improvement in survival, prolongation of delay or maternal complications. Zhang et al. retrospectively analyzed 7 cases that were offered cervical cerclage after delivery of the first twin and found that the procedure did not increase the risk for intrauterine infection (13).

In a retrospective analysis of 20 cases by Doger E, conclusion was that cervical cerclage after the first delivery is associated with a longer delivery interval and higher birth weight of retained fetus(14)

Conclusion

With increasing use of ART and consequent multifetal gestation, delayed interval delivery rates are expected to increase in coming years. Better antenatal surveillance and new tocolytic agents are becoming more popular. Elective cerclage may be considered in twin pregnancies with delivery of the first twin before 23 weeks of gestation.

References

1. Carson JL. Twins born with an interval of forty-four days. Br Med J. 1880;1:242.
2. Abrams R. H. Double pregnancy; report of a case with thirty-five days between deliveries. Obstetrics &Gynecology. 1957;9(4):435–438.
3. Drucker, P., Finkel, J. and Savel, L.E. (1960) Sixty-five days interval between the birth of twins: a case report. Am. J. Obstet. Gynecol., 80, 761–763. E
4. J. AdetunjiAdeleye, Retained second twin in lbadan: Its fate and management September 15, 1972 American Journal of Obstetrics and Gynaecology.
5. EicherW. 72 TaegiggegeburtspausebeiZwillingen. Muench Med Wochenschr 1970; I 12:422.
6. Thomson, RJ (1978): Delayed interval delivery of a twin pregnancy. ObstetGynecol 52 (suppl): 37s–40s
7. Porreco RP1, Sabin ED, Heyborne KD, Lindsay LG.Delayed-interval delivery in multifetal pregnancy.Am J Obstet Gynecol. 1998 Jan;178,20-3.
8. Farkouh LJ1, Sabin ED, Heyborne KD, Lindsay LG, PorrecoRP.Delayed-interval delivery: extended series from a single maternal-fetal medicine practice. Am J Obstet Gynecol. 2000 Dec;183(6):1499-503
9. Feys S, Jacquemyn Y. Delayed-interval delivery can save the second twin: evidence from a systematic review. Facts Views Vis Obgyn. 2016;8(4):223–231
10. Arabin B, Eyck J. Delayed-interval delivery in twin and triplet pregnancies: 17 years of experience in 1 prenatal center. Am J Obstet Gynecol. 2009;200:154.e1–154.e8
11. Arias F. Delayed delivery of multifetal pregnancies with premature rupture of membranes in the second trimester. Am J Obstet Gynecol. 1994;170:1233–1237.
12. Fayad S, Bongain A, Holhfeld P, et al. Delayed delivery of second twin: a multicenter study of 35 cases. Eur J ObstetGynecolReprod Biol. 2003;109:16–20.
13. Zhang J, Johnson CD, Hoffman M. Cervical cerclage in delayed interval delivery in a multifetal pregnancy: a review of seven case series. Eur J ObstetGynecolReprodBiol 2003;108:126–30.
14. Doger E, Cakiroglu Y, Ceylan Y, et al. Obstetric and neonatal outcomes of delayed interval delivery in cerclage and non-cerclage cases: An analysis of 20 multiple pregnancies. J ObstetGynaecol Res. 2014;40:1853–1861.

Case Report – Reactivation of pelvic tuberculosis following endometrioma aspiration ?

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Mrs. A, 34 year old female, married for 10 years with primary infertility and a known case of recuurent endometriosis presented at our centre for ART treatment.There was nothing significant in her family history. Her past history was very doubtful for suspectedlung tuberculosis in childhood though she never received any ATT. Husband's semen analysis was normal. She had regular monthly menstrual cycles with moderate to severe dysmenorrhea relieved with oral and sometimes intravenous analgesics. She was diagnosed to have B/L endometriosis on USG 9 years back while being investigated for severe dysmenorrhea . Her first laproscopy, which was done 6 months after diagnosis , revealed Grade 2-3 endometriosis with bilateral patent tubes. Bilateral endometriomas were removed and she was given GnRH agonist once a month for 3 cycles. HPE from ovarian tissue suggested only endometriosis while AFB culture and PCR from endometrial currettings was normal. Over the next 6 to 7 years, she was given 6 to 7 cycles of IUI, ovulation induction being done by oral ovulogens along with gonadotropins. Her Day 2/3 hormones – FSH, LH , estradiol levels were never checked. Her follow up scans during this treatment suggested of ovulation, though each ovary had endometriomas around 5-6 cm each with 1 -2 AFC. Shewas taken for a second laproscopy because of intermittent bouts of moderate to severe pain abdomen. A relook laproscopy revealed a frozen pelvis and no exploration was attempted. She was advised for IVF. During her work up for IVF, her FSH was 16 with an AMH of 0.1. She was advised for a donor egg programme in view of poor ovarian reserve. Before enrolling her for egg donor programme, B/L endometriomas were drained done P/V and she was put on a long protocol in the subsequent cycle.However since the waiting period was too long for the egg donor programme she decided to change the centre and was referred to our centre. All her Pre–ivf investigations for egg donor programme were normal except that her USG again showed appearance of B/L endometriomas of 6 to 7 cm each. She was started with HRT for endometrial preparation. On day 12 of progynova when she came for follow up, she complained of moderate to severe pain lower abdomen intermittently since 4 days, for which she had to take analgesics. There were no other accompanying symptoms. Her USG showed an endometrial thickness of 8.4 mm triple layer with same findings in B/L ovaries with no fluid in pelvis. P/A examination revealed soft abdomen with mild diffuse tenderness but no organomegaly. She was afebrile and her vitals were stable. Considering her signs and symptoms, a detailed discussion was done with the couple and conscious decision to abandon the cycle was taken. She was advised admission for observation and detailed work up, to which she refused. However she was put on broad spectrum antibiotics. CBC , RFT , LFT, chest X-ray and USG whole abdomen was advised and she was asked to follow with reports the next day. The same evening patient had a bout of severe pain abdomen for which she got admitted to a nearby private nursing home. There she was diagnosed as a case of OHSS based on her history and USG findings of B/L ovarian cysts with mild free fluid in POD and was treated for the same (forgetting the fact that she was undergoing endometrial preparation only and that no ovulation induction was done). When her pain abdomen worsened inspite of i/v analgesics she was referred back to our centre. On admission she had 101 fever with a haemoglobin of 8.0 mg/dl, TLC 16000, neutrophils 75%, lymphocytes 15% and ESR of 44. Her blood pressure was 90/50 and a pulse rate 110/mt . P/A examination revealed diffuse tenderness, guarding and rigidity She was diagnosed clinically as a case of peritonitis. USGshowed haemorragic fluid in the pelvic cavity with B/L endometriomas. An urgent laparotomy was done. Per op findings revealed B/L TO masses with ruptured endometriotic cysts with abscess, with tubercles on the TO masses. TO masses were removed and an abdominal lavage was done. Post op she was managed with antibiotics and ATT was started based on lapratomy findings. Fortunately, she recovered and was discharged in 2 weeks . Her AFB culture of peritoneal fluid was positive for tuberculosis. HPE of the tubercles showed granulomatous lesions suggestive of tuberculosis.

She was continued on ATT for 9 months. Patient recovered fully but took a decision not to attempt an IVF.

Discussion And Review Of Literature

This case is being presented because of diagnostic dilemma based on clinical presentation and ultrasound findings . Endometriosis is found in 25-40% of infertile women, as compared to 2-5% of the general population (1) and genital tuberculosis (GTB) mostly affects young women between 20 and 40 years of age and is relatively common in developing countries (2).

During primary tubercular infection, there may be systemic redistribution of M. tuberculosis and later on this may get reactivated leading to pelvic tuberculosis (3-4). Tubercular pelvic disease may present as an adnexal mass, ascites or both and can be difficult to distinguish from other PID causes (5).

Increased susceptibility to infection in women with endomeriosis may lead to the development of TOA [6] because of the altered immune environment seen with abnormally placed endometrial glands and stroma (7). Following transvaginal ovum retrieval or aspiration of endometrioma the evidence suggest that the presence of old blood in the endometrium provide a medium for bacterial growth and hence a risk for pelvic inflammation of abscess formation(8). Infection in an endometrioma following percutaneous fine needle aspiration in a 16 year old girl has been reported by Martino et al (9).

Interestingly, in this case report, the patient's P/V aspiration of B/L endometriomas took place about three months prior to clinical presentation and it seems to be the cause for abscess formation and flare up of tuberculosis. Himabindue et al in 2008 , reports a somewhat similar case of pelvic tuberculosis reactivation following in vitro fertilization. (10).
Coexisting endometriosis and tuberculosis of ovaries is very rare and has a greater impact on fertility. It may also alter clinical and radiological/ ultrasonological features, leading to difficulty in diagnosis and treatment (11), as seen in the present case. Unfortunately in our case, the silent rupture of tubo-ovarian mass was missed because of the unusual presentation. A case has been reported where tubercular ascites simulated ovarian hyperstimulation following IVF and embryo transfer pregnancy (12) but in our case since there was no ovulation induction the possibility of OHSS should have been avoided as this probably would have saved some precious time and a timely intervention would have been done. Coexisting endometriosis and tuberculosis was diagnosed only intraoperatively on the basis of ovarian tubercles and postoperatively, on the basis of HPE and positive AFB culture.

Though the patient improvedand recovered with postoperative antitubercular therapy, early diagnosis by proper surgical exploration and adequate treatment could have improved the chances of conception and would have also minimized morbidity.

References:

1. McLeod BS, Retzloff MG. Epidemiology of endometriosis: an assessment of risk factors. Clin Obstet Gynecol. 2010;53:389–396.
2. Jindal UN, Bala Y, Sodhi S, Verma S, Jindal S. Female genital tuberculosis: early diagnosis by laparoscopy and endometrial polymerase chain reaction. Int J Tuberc Lung Dis. 2010;14:1629–1634.
3. Insight into the diagnosis and management of subclinical genital tuberculosis in women with infertility - Nalini Mahajan, Padmaja Naidu, Simran Deep KaurJ Hum Reprod Sci. 2016 Jul-Sep; 9(3): 135–144.
4. Monif GRG. Tuberculosis. In: Infectious Diseases in Obstetrics and Gynecology. 3rd ed. Omaha: IDI Publications; 1993:395-411.
5. Iylhan AH, Durmusxoglu F. Case report of a pelvic-peritoneal tuberculosis presenting as an adnexal mass and mimicking ovarian cancer, and a review of the literature. Infect Dis Obstet Gynecol 2004;12:87–9.
6. Annamraju H, Ganapathy R, Webb B. Pelvic tuberculosis reactivated by in vitro fertilization egg collection? Fertil Steril. 2008;90:2003.
7. Chen M-J, Yang J-H, Yang Y-S, Ho H-N. Increased occurrence of tubo-ovarian abscesses in women with stage III and IV endometriosis. Fertility and Sterility. 2004;82(2):498–499.
8. Lebovic DI, Mueller MD, Taylor RN. Immunobiology of endometriosis. Fertility and Sterility. 2001;75(1):1–10.
9. Moini A, Riazi K, Amid V, Ashrafi M, Tehraninejad E, Madani T, et al. Endometriosis may contribute to oocyte retrieval-induced pelvic inflammatory disease: report of eight cases. J Assist Reprod Genet. 2005;22:307–309.
10. Martino CR, Haaga iR, Brvan Pi. Secondary infection of an endornetrioma following tine-needle aspiration. Radiology., 1984: 151: 53-4.
11. Himabindu Annamraju, Ramesh Ganapathy, Bev Webb et al. Pelvic tuberculosis reactivated by in vitro fertilization egg collection? Fertility and Sterility Vol. 90, No. 5, November 2008
12. Ghosh SB, Mala YM, Tripathi R, Tyagi S. Coexisting genital tuberculosis and endometriosis presenting as abdominal mass in an infertile woman: a report of a rare case. Fertil Steril. 2008;90:443.
13. Amar Ramachandran, Pratap Kumar, Naveen Manohar, Raviraj Acharya, Anita Eipe, Rajeshwari G. Bhat, Lorraine Simone Dias, Padmaja Raghavan et al.
Tubercular Ascites Simulating Ovarian Hyperstimulation Syndrome following In Vitro Fertilization and Embryo Transfer Pregnancy.
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Critical ovarian hyper stimulation syndrome after GnRH agonist trigger given for final oocyte maturation in IVF cycle: Search for a putative cause through a literature search.

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A 32-year-old patient presented three days after oocyte retrieval with complaints of giddiness, increasing abdominal pain and distension, breathlessness and reduced appetite. She also gave history of reduced frequency and volume of micturition since one day. There was no history of vaginal bleeding, fever or altered bowel habits.

She was a known case of secondary infertility having oligomenorrhoiec hyper and rogenic polycystic ovarian syndrome. One previous spontaneous conception had resulted in an ectopic pregnancy that was managed conservatively. Investigations had revealed, normal semen analysis, unilateral tubal block, normal uterine cavity and endometrium and polycystic ovaries on ultrasound. Four intrauterine inseminations and one in-vitro-fertilization (IVF), resulting in a biochemical pregnancy loss, had been attempted prior to the present procedure. Her pre-treatment body mass index was 26.4Kg/m^2.

This IVF procedure involved controlled ovarian stimulation (COS) with recombinant follicle stimulating hormone (FSH) in an antagonist protocol. 200IU of rec FSH was the starting dose that was decreased to 150 units and 75 units on day 6 and 8 of stimulation respectively. Thus she received a total dose of 1450 IU over nine days. Final oocyte maturation was triggered with gonadotropin releasing hormone agonist(Inj Triptorelin 0.2mg subcutaneously) in view of a hyper-stimulated ovary and estradiol levels of 6183 pg/ml on trigger day. 31 oocytes were retrieved in a rather difficult transvaginal retrieval procedure as a result of high placement of one ovary. Eight follicles of sizes 12-20 mm were left unaspirated due to difficult access through both the transabdominal and transvaginal route. Intravaginal bromocriptine in dose of 2.5mg per day and injection cetrorelix acetate 0.25mg per day were prescribed from the day of retrieval.

The symptoms mentioned above developed from the same day and worsened 3 days later (5 days after the GnRH agonist trigger). Initial assessment revealed tachypnoea, pulse rate of 100beats per minute, blood pressure of 130/80mm Hg, no pallor, clear chest and abdominal distension with positive fluid thrill. Investigations revealed haemoconcentration, (PCV: 47%, TLC: 15,100) hypoproteinemia, hyponatremia, hyperkalemia, normal liver enzymes and blood clotting parameters. USG showed gross ascites and bilateral multi-cystic ovarian enlargement to 15x11cm and 10.5x9.5cm.

A provisional diagnosis of early onset severe ovarian hyperstimulation syndrome (OHSS) was made and management initiated with a judicious combination of intravenous crystalloids and colloids in order to maintain a urine output of upto 50ml/hour. Ultrasound guided paracentesis was undertaken to improve symptoms of breathlessness and oliguria; subcutaneous low molecular weight heparin was started daily as thomboprophylaxis. The patient developed severe breathlessness with oxygen saturation of 70% on day2 of admission, for which she was shifted to the intensive care unit. Chest X ray suggested early consolidation. Bedside echocardiography was normal.10mg of frusemide injection aided in reducing breathlessness. sA total of three abdominal paracentesis were done on days 3, 4 and 6 of OCR amounting to 2liters, 2.5liters and 1.75 liters of clear ascitic fluid. Fluid administration was done under central venous pressure monitoring. Symptoms and clinical features began to settle by day 4 of admission (day8 of agonist trigger) and the patient was discharged in a stable state two days later. Seven blastocysts had been cryo preserved and she underwent frozen embryo transfer in a hormonally replaced cycle. She has an ongoing pregnancy of 26 weeks at present.

Discussion

In IVF/ICSI cycles, exogenous human chorionic gonadotropin (hCG) has been used for years as a substitute for the naturally occurring LH surge to trigger final oocyte maturation. Because of its longer half-life, it is associated with a higher risk of OHSS especially in high-risk women. The incidence of OHSS in controlled ovarian stimulation cycles is estimated to be 20-30% in its mild form and 3-8% in moderate to severe form.[1] In the modern practice however, the incidence of severe ovarian hyper stimulation syndrome requiring inpatient care has been steadily going down, perhapsas a result of transition to antagonist protocols[2] and estimated to be between2-3%.[3,4]

Gonadotropin releasing hormone agonist (GnRHa) as a triggering agent for final follicular maturation was proposed in 1992.[5] GnRHa induces a shorter and more natural pre-ovulatory gonadotropin surge (for 24-36 h) in contrast to hCG (5 days) by stimulation of the pituitary LH secretion. This is expected to eliminate sustained stimulation of corpus luteal cells, which then reduce their output of steroidal hormones and vascular endothelial growth factor, the pathognomonic cytokine of OHSS. The agonist as a trigger can only be used in COS protocols where the pituitary continues to be sensitive to its action such as in antagonist protocol IVF. A GnRH agonist protocol would hence preclude its use.

Cohort studies, controlled trials and systematic review of controlled trials have established that amongst high risk women undergoing IVF, GnRH agonist in comparison to hCG injection as a final oocyte maturation trigger, drastically brings down or even eliminates the occurrence of severe OHSS.[6,7,8,9,10,11,12,13,14] The confidence in its effectiveness to eliminate severe OHSS is so great that in combination with a freeze-all strategy, GnRH agonist trigger has been proposed as a measure for creating OHSS free clinics.[15]

However, even as the extreme confidence in GnRH agonist trigger in OHSS prevention soars, sporadic reports of severe OHSS with its use have surfaced since 2013 involving a total of ten women.[16,17,18,19] All described reports have involved women undergoing IVF in antagonist protocols, who received GnRH agonist trigger because they were at high risk for OHSS development based on ultrasound and hormonal picture. To prepare the uterus for fresh embryo transfer, six of these women received 1500 IU hCG on OCR day, and one received naferelin acetate twice daily from the day of oocyte retrieval. Both these agents served as additional stimulants of sensitized corpus luteal cells to cause sustained VEGF secretion. So these seven women had reasons to develop OHSS despite GnRH agonist being used as a triggering agent.

In the remaining three cases, (16, 18) no inciting agent was administered and embryo transfer was withheld. Authors have speculated the role of GnRH receptor, FSH receptor, or LH receptor gene mutations in the development of OHSS in these two reports (16, 18).
All early cases resolved within 4-5 days of presentation.
The present case had oligomenorrhoiec PCOS, received a BMI-appropriate total gonadotropin dose, was triggered with GnRH agonist instead of hCG, received no rescue hCG or GnRH agonist in the luteal phase and underwent a freeze-all strategy as OHSS preventive measures. The development of early onset severe OHSS despite this begs for an answer. One reason could be that eight follicles (~20% of the total) between 12 and 20mm were left unaspirated due to difficult access transvaginally and trans-abdominally. It was supposed that this might have lead to an increased burden of follicular cells contributing to VEGF secretion. Follicular aspiration of smaller follicles prior to hCG injection was practiced as a measure of OHSS prevention in the nineties in some centres[20] although the practice was found to be as effective or ineffective as coasting.[21] However it did not find a place of virtue in any subsequent reviews on OHSS prevention measures and was largely abandoned. Having said that, one does not know if aspirating these follicles, in this case would have prevented or lowered the intensity of the syndrome.

The other possibility could be what stares us in the face. That GnRH agonist does not lead to an absolute elimination of severe OHSS. This could have to do with an LH or FSH receptor mutation that allows it be activated for a prolonged time long after the LH peak induced by GnRH agonist has subsided.

Conclusions

This case report adds to the few reported cases in literature of severe OHSS developing after GnRH agonist use as a triggering agent in high risk women undergoing COS for IVF. One needs to be wary of this fact and strive towards a controlled stimulation aiming at the development of not more than 15-20 follicles.

Table 1: Severe OHSS cases reported after GnRH agonist trigger in IVF cycles

Case Report, year	Pa-tients	Patient profile	Stimulation regime	IVF cycle details+treat-ment from OCR day	presen-tation day (post OCR)	PCV/TLC at presen-tation	Abdom-inal tapping	Reso-lution day (post OCR)
Seyhan et al 2013 **(6 cases)**	Case 1	27 yrs. Oligo-menorrhoiec PCOS, 31.2 Kg/m2 IVF for male factor	Recombinant FSH, Total Dose: 1725 over 8 days E2: 5589 pg/ml Trigger Buserelin,	OCR: 65 M2: 41 Cabergoline 0.5mg once a day 1500 IU hCG on the day of OCR freeze -all	3	PCV: 53% TLC: 21,100 Tense asci-tes oliguria	Yes	6
	Case 2	31 yrs, eumen-orrhoeic, BMI 29.1Kg/ m2	Rec FSH dose: 1500IU over8 days Serum E2: 2653pg/ml Trigger: Buserelin	OCR: 53 M2: 32, Cabergoline 0.5mg once a day 1500 IU hCG on the day of OCR freeze -all	3	PCV: 51% TLC: 23,380 Moderate ascites	Yes Day5 and 7	9

	Case 3	33 yr eumen-orrhoeic,	Recombinant FSH: total dose: 975 IU E2: 3011pg/ml Trigger: DEca-peptyl	OCR: 33 M2: 18 1500 IU hCG on the day of OCR freeze -all	3	PCV: 54% Moderate ascites	No	6
	Case 4	31 yr old PCOS BMI: 32.6 Kg/ m2	Recombinant FSH Total dose: 1400 over 8 days, E2: 8364 pg/ml Coasting for 2 days Trigger: buserlin	OCR: 26 M2: 23 1500 IU hCG on the day of OCR 2 embryos transferred on 3rd day (negative result)	6	PCV: 49% TLC: 18,000	No	8
	Case 5	30 yr, PCOS BMI: 31 Kg/ m2	Recombinant FSH: Total dose: 1200IU over 8 days Coasting for 2 days E2: 6814pg/ml GNRH agonist on day 10	OCR: 23 M2: 14 1500 IU hCG on the day of OCR 2 embryos transferred on day 3 (negative result)	3	PCV: 46.5% WBC: 18,900	Yes	6
	Case 6	27 yrs. Eumenor-rhoeic IVF for male factor	Rec FSH: total dose 1088 IU E2: 4959	OCR: 50 M2:35 1500 IU hCG on OCR day, Fresh blastocyst transfer, Miscarriage at 8 weeks	9	Haemocon-centration, 600ml ascites	No	14
Fatemi et al 2014	Case 1	29 yrs, Eu-menorrhoeic, BMI: 25.3Kg/ m2 IVF for prima-ry unexplained infertility	Rec FSH: Total: 1350 IU over 9 days E2: 4300pg/ml decapeptyl trigger	30 oocytes, 28 oocytes cryo-preserved. No transfer	1	PCV: 50% TLC:15,500 ovarian size 7 cm, 7cm ascites oliguria	Yes	6
	Case 2	27 yr, eumen-orrhoiec, egg donor	Rec FSH: Total: 1687.5 IU over 9 days, E2: 3578 pg/ml Leuprolide trigger	30 oocytes, 22 donated	6	PCV: 47% TLC: 18,100 Ovaries: 7/8cm ovary ascites, oliguria	Yes	10
Mahajan et al 2017	1	33 yr, 28.6 Kg/m2, PCOS, AMH: 27ng/ ml IVF for male factor	hMG: Total: 2050 IU E2: 10,045 pg/ ml, Leuprolide 1 mg	37 M2, 20 fertilized freeze all Cabgolin (0.5 mg) GnRH antagonist	1	PCV: 46% TLC: 12,500/ cmm	No	4
Friedler & Grin 2019	1	36 yr old oligomenor-rhoiec PCOS, BMI: 24Kg/ m2	E2: 3299 Trigger: triptore-lin 0.2mg	OCR: 16 M2: 14 Naferelin actate 200mcg BD from the day of OCR Fresh Embryo transfer on day5, Ongoing pregnancy of 34 weeks	6	PCV: 44% Ovaries: 8cm/8cm	Yes (Twice)	18
Satwik R 2019	1	33 yr, oligo-menorrhoiec PCOS, BMI: 26.4Kg/m2, IVF for uni-lateral tubal block with previous failed IUIs	Rec FSH Total: 1450 IU/ml over 9 days, deca-peptyl trigger	31 oocytes, 7 blastocysts, freeze all, do-pamine agonist, antagonist	3	PCV: 47.1%, TLC: 14,400 tense asites, oliguria, ovaries: 15/10.5 cm	Yes (thrice)	10

BMI: Body mass index; OCR: Oocyte Retrieval, PCV: Packed cell Volume in %; TLC: Total leukocyte count: per cubic mm

Table 2: Haematological, biochemical and ultrasound parameters on OCR day, admission and discharge day

	Haemoglo-bin Gm%	PCV %	TLC / cubic mm	Total proteins Gm/dL	Serum Albumin gm/dL	Weight Kg	Ascites	Ovarian size (larg-est diameter)
OCR day	12.1	35.8	9100	-	-	66	Fluid in POD	9 cm and 5cm (after OCR)
Day of pre-sentation (day 3 post OCR)	15.7	47.1	14,400	2.8	1.44	70Kg	Tense ascites	15cm and 10.5cm
Day of dis-charge (day 10 post OCR)	10.9	33.1	7140	4.71	3.08	67Kg	Moderate Fluid in POD, flanks, morri-son's pouch	13cm and 8cm

Reference

1. Mourad S, Brown J, Farquhar C. Interventions for the prevention of OHSS in ART cycles: an overview of Cochrane reviews. Cochrane database Syst Rev. 2017. CD012103
2. Lin H, Li Y, Li L, Wang W, Yang D, Zhang Q. Is a GnRH antagonist protocol better in PCOS patients? A meta-analysis of RCTs. PLoS One. 2014;9(3):e91796. Published 2014 Mar 18. doi:10.1371/journal.pone.0091796
3. Papanikolaou EG, Tournaye H, Verpoest W, Camus M, Vernaeve V, Van Steirteghem A, Devroey P. Early and late ovarian hyperstimulation syndrome: early pregnancy outcome and profile. Hum Reprod. 2005 Mar;20(3):636-41.
4. Mekaru K, Yagi C, Asato K, Masamoto H, Sakumoto K, Aoki Y. Comparison between the gonadotropin-releasing hormone antagonist protocol and the gonadotropin-releasing hormone agonist long protocol for controlled ovarian hyperstimulation in the first in vitro fertilization-embryo transfer cycle in an unspecified population of infertile couples. Reprod Med Biol. 2011;11(2):79–83. Published 2011 Sep 21. doi:10.1007/s12522-011-0109-2
5. Segal S, Casper RF. Gonadotropin-releasing hormone agonist versus human chorionic gonadotropin for triggering follicular maturation in in vitro fertilization. Fertil Steril. 1992 Jun; 57(6):1254-8.
6. Hwang JL, Chen SU, Chen HJ, Chen HF, Yang YS, Chang CH et al. Feasibility of corifollitropin alfa/GnRH antagonist protocol combined with GnRH agonist triggering and freeze all strategy in polycyctic ovary syndrome patients. J. Formos. Med. Assoc. 2018 Jun; 117 (6):535-540
7. Krishna D, Dhoble S, Praneesh G, Rathore S, Upadhaya A, Rao K. Gonadotropin-releasing hormone agonist trigger is a better alternative than human chorionic gonadotropin in PCOS undergoing IVF cycles for an OHSS Free Clinic: A Randomized control trial. J Hum Reprod Sci. 2016 Jul-Sep;9(3):164-172.
8. Kol S. Prediction of ovarian hyperstimulation syndrome: why predict if we can prevent! Hum Reprod. 2003;18(7):1557–8.
9. Orvieto Raoul. Can we eliminate severe ovarian hyperstimulation syndrome? Human Reproduction. 2005;20(2):320–322.
10. Humaidan P, Bredkjaer HE, Bungum L, Bungum M, Grondahl ML, Westergaard L, et al. GnRH agonist (buserelin) or hCG for ovulation induction in GnRH antagonist IVF/ICSI cycles: a prospective randomized study. Hum Reprod. 2005;20(5):1213–20.
11. Engmann L, DiLuigi A, Schmidt D, Nulsen J, Maier D, Benadiva C. The use of gonadotropin-releasing hormone (GnRH) agonist to induce oocyte maturation after cotreatment with GnRH antagonist in high-risk patients undergoing in vitro fertilization prevents the risk of ovarian hyperstimulation syndrome: a prospective randomized controlled study. Fertil Steril. 2008;89(1):84–91.
12. Galindo A, Bodri D, Guillen JJ, Colodron M, Vernaeve V, Coll O. Triggering with HCG or GnRH agonist in GnRH antagonist treated oocyte donation cycles: a randomised clinical trial. Gynecol Endocrinol. 2009;25(1):60–6
13. Humaidan P, Kol S, Papanikolaou EG. GnRH agonist for triggering of final oocyte maturation: time for a change of practice? Hum Reprod Update. 2011;17(4):510–24
14. Youssef MA, Van der Veen F, Al-Inany HG, Mochtar MH, Griesinger G, Nagi Mohesen M, Aboulfoutouh I, van Wely M. Gonadotropin-releasing hormone agonist versus HCG for oocyte triggering in antagonist-assisted reproductive technology. Cochrane Database Syst Rev. 2014 Oct 31;(10):CD008046.
15. Devroey P, Polyzos NP, Blockeel C. An OHSS-Free Clinic by segmentation of IVF treatment. Hum Reprod. 2011 Oct;26(10):2593-7
16. Fatemi HM, Popovic-Todorovic B, Humaidan P, Kol S, Banker M, Devroey P, García-Velasco JA. Severe ovarian hyperstimulation syndrome after gonadotropin-releasing hormone (GnRH) agonist trigger and "freeze-all" approach in GnRH antagonist protocol. Fertil Steril. 2014 Apr;101(4):1008-11
17. Seyhan A, Ata B, Polat M, Son WY, Yarali H, Dahan MH. Severe early ovarian hyperstimulation syndrome following GnRH agonist trigger with the addition of 1500 IU hCG. Hum Reprod. 2013 Sep;28(9):2522-8.
18. Mahajan N, Gupta S, Sharma S, Rani K, Naidu P, Arora PR. Early onset ovarian hyperstimulation syndrome despite use of segmentation approach and ovarian hyperstimulation syndrome prophylaxis. J Hum Reprod Sci. 2015;8(4):234–238. doi:10.4103/0974-1208.170415
19. Friedler S, Grin L. Luteal phase support with GnRH agonist does not eliminate the risk of ovarian hyperstimulation syndrome. Gynecol. Endocrinol. 2019 Jan 07: 1-2
20. Gonen Y, Powell WA, Casper RF. Effect of follicular aspiration on hormonal parameters in patients undergoing ovarian stimulation. Hum Reprod. 1991 Mar;6(3):356-8
21. Egbase PE, Sharhan MA, Grudzinskas JG. Early unilateral follicular aspiration compared with coasting for the prevention of severe ovarian hyperstimulation syndrome: a prospective randomized study. Hum Reprod. 1999 Jun;14(6):1421-5

Unusual Case Of Genuine Empty Follicle Syndrome

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Case Study:

A 34 year old lady presented with history of secondary infertility in January 2018. She was married for 14 years and had conceived spontaneously after 1 year of marriage which culminated in full term normal vaginal delivery of a healthy female child. After 4 years of child birth she started trying for second child but her menstrual cycles had become irregular, she had gained weight and was diagnosed with PCOS . She was advised to lose weight and went through few cycles of ovulation induction with oral drugs. She conceived again after 2 years on ovulation induction but it ended up with missed abortion for which suction and evacuation was done . After 1 year of abortion she again started trying with ovulation induction, five cycles of IUI out of which two were with gonadotropins failed over a period of two years. She also went through laparoscopy and hysteroscopy in September 2017 where uterus and tubes were found to be normal and bilateral free spill was documented. Bilateral ovarian drilling was also done. In view of prolonged secondary infertility with multiple failed ovulation induction and IUI cycles, couple was finally taken up for IVF in February 2018 after appropriate counseling.

At the time of entry into IVF cycle she was getting regular cycles for last 6 months, her BMI was 23.8 Kg/m2 and AMH was 6 ng/ml. She was taking metformin 1700 mg of Metformin daily in two divided doses.

First cycle: Patient was taken up for antagonist protocol with 200 units as starting dose of gonadotropin (Rec FSH). After 5 days of stimulation cetrotide 0.25 mg was added. The dose of gonadotropin was brought down to 150 units after 7 days due to signs of hyperstimuation . After 10 days of stimulation patient was ready for final trigger but she had more than 20 follicles in each ovary and final estradiol level was 4800 pg/ml hence Inj Leuprolide 2 mg was given as trigger to prevent ovarian hyperstimulation syndrome. After 36 hours of Inj Leuprolide patient was taken up for oocyte retrieval. Approximately 40 follicles were aspirated in total but only two OCCs were retrieved from which on denudation grossly abnormal and degenerated oocytes were found. Her serum LH was sent and value came out to be 22 IU/L .

Second cycle: The couple was counseled and taken up for second cycle after menses. A few modifications were made in this cycle. It was antagonist protocol again, a Rec FSH (from a different company) was started in the dose of 150 units daily. After 5 days of stimulation the follicular recruitment was less hence along with cetrotide Rec LH was added in the dose of 75 units daily and was continued till the end. After 10 days of stimulation she was ready for oocyte retrieval but again showed multiple follicles with estradiol level was 4650 pg/ml. The patient was given dual trigger this time with 125 µg of Rec HCG and 0.2 mg of Triptorelin this time and oocyte retrieval was planned after 36 hours. In this cycle also more than 30 follicles were aspirated but no occ's were retrieved. After aspirating one ovary urine HCG test was done which was positive hence the other ovary was also aspirated with follicular flushing with double lumen needle. Her serum β HCG taken at the time of retrieval was found to be 80 IU/L .

The Dilemma !

A young woman who had conceived twice earlier with one live birth seemed to be suffering form genuine Empty Follicle Syndrome (gEFS) in two consecutive optimally stimulated IVF cycles!

Review of Literature:

EMPTY FOLLICLE SYNDROME

Empty follicle syndrome (EFS) is defined as complete failure to retrieve oocytes during oocyte aspiration in an optimally stimulated cycle with multiple follicles and appropriate estradiol levels. Most cases of EFS in clinical practice are actually false EFS which occurs due to either ovulation trigger not performed or technical error in the procedure of oocyte retrieval. Patients may take ovulation trigger at wrong time or even wrong day! They may make mistake in dissolving the drug in the solvent or may spill it or rarely there could be a problem with the batch of HCG. During the procedure if aspiration pressure is not maintained or the inexperience clinician does not completely aspirate the follicles it may end up with no oocytes. Genuine EFS occurs if there is complete failure to retrieve oocytes even when ovulation trigger has performed. To distinguish between the two variants of EFS serum HCG concentration is measured immediately when one fails to retrieve oocytes. In literature a wide range (5- 160 IU/L) of HCG has been described by different investigators as concentration threshold after 36 hours of exogenous HCG administration. When GnRH agonist is used as trigger in hyper-stimulated patients serum LH needs to be monitored and unfortunately no clear cut-off has been given so far. Some studies have described circulating LH level of 15 IU/L as threshold value.

INCIDENCE OF EFS:

A wide range of prevalence of EFS , 0.045%to 7% of IVF cycles has been reported which reflects the uncertainity in its diagnosis. Serum HCG concentration is usually used to distinguish between genuine and false EFS. Mesen et al (2011) reported the incidence of genuine EFS as 0.011% (2 cases out 18,294 cycles) hence genuine EFS is indeed a rare entity! Studies have shown that prevalence of EFS is comparable in both antagonist and GnRH agonist long protocol. Earlier it was thought that older women and those with low ovarian reserve were more prone to EFS but many investigators later demonstrated similar rates of EFS in oocyte donors who essentially have good ovarian reserve.

AETIOLOGY OF GENUINE EFS:

Genuine EFS is a very intriguing situation and many researchers have worked on its poorly understood pathophysiology. Granulosa cells of patients with recurrent EFS have been reported to have increased expression of pro-apoptotic genes and reduction in factors responsible for normal follicular growth. Genuine EFS has been associated with mutation in genes coding for LH/ HCG receptor(LHCGR) which renders the follicles unresponsive to HCG trigger. A pericentric inversion on fragile site of chromosome 2 has also been linked with genuine EFS and since genes on chromosome 2 code for premature ovarian ageing also an association between the two has been suggested.

MANAGEMENT OF GENUINE EFS:

Since false EFS is due to inappropriately given HCG trigger, it is logical to either give a second trigger and rescue rest of the follicles (if not already aspirated) in the same cycle or repeat a second cycle with carefully timed HCG trigger. Management of Genuine EFS is a challenge because the pathophysiology is not clear. Different strategies have been tried with very modest results.

1. Performing oocyte retrieval after 36 hours of HCG trigger in order to prolong the exposure of HCG has been tried but with unsatisfactory outcome.
2. Rescue dose of HCG has been tried in Genuine EFS also but with very limited efficacy.
3. A more physiological trigger in the form of GnRH agonist may paradoxically benefit in few cases where more pharmacological HCG doesnot work.
4. On the other hand where EFS occurred with GnRH agonist trigger , HCG may be tried as rescue or in next cycle .
5. Successful outcome has been reported in a case of repeated EFS with dual triggering i.e. GnRH agonist plus HCG in which GnRH agonist was given 40 hours and HCG 36 hours prior to oocyte aspiration. Dual trigger has been associated with better oocyte quality and embryo quality by different authors. More studies are required to ascertain the role of dual trigger in genuine EFS.

MANAGEMENT IN OUR CASE…

The above case was essentially genuine EFS since the serum LH level when GnRH agonist trigger was given and serum HCG when dual trigger was given were both above the cut offs . Our patient was a hyper-responder and despite adequate dose of FSH she hyper-stimulated in both the cycles. After the failure to retrieve oocytes in first cycle we made some changes in the second cycle; LH was added in stimulation, dual trigger was given (though the dose of recHCG was kept at 125 to avoid OHSS) and oocyte aspiration was done at 36 and half hours after retrieval. Still we failed to obtain oocytes in second cycle. What was more intriguing in this case was that the patient had conceived on her own in past . Punhani R et al (2016)published an Indian case series of 11 patients of EFS but they all were primary infertility. In a systematic review of case series of EFS, 83% cases of genuine EFS were primary infertility. In this case we finally gave the couple an option of donor oocytes .

Suggested reading:

1. Rivelli A, Carosso A, Grassi G et al. Review - Empty follicle syndrome revisited: definition, incidence , early diagnosis and treatment. RBM On line 35 (2017): 132-138.
2. Deepika K, Rathore S, Garg N, Rao K . Empty follicle syndrome: Successful pregnancy outcome after dual trigger. J Hum Reprod Sci 2015;8:170-4.
3. Punhani R, Shankar K, Varma TR. Empty follicle Syndrome : Case series and review of literature. IVF lite.2016;3:52-7.
4. Stevenson TL, Lashen H et al. Empty follicle syndrome: the reality of a controversial syndrome, a systematic review. Fertil Steril 2008;90(3):691-98.

IFS – A commitment to Education, Training and Research

FROM THE DESK
ADVOCACY COMMITTEE

DR SONIA MALIK
Convenor
Advocacy Committee, IFS
Past President, IFS

The committee was constituted during the tenure of the present President Dr Gouri Devi with the purpose of advocating the ideology and the governing principles of IFS to other professional groups and public at large.

Activities.

1. Proposed amendaments to the upcoming Surrogacy bill strongly putting our view point and objections. This was drafted with the help of our IFS lawyer and sent to the Ministry of Health & Family Welfare and ICMR. The meeting was convened by Dr Gouri Devi President and Dr PankajTalwar Sec. Gen. IFS.
2. A meeting was convened by DrKaminiRao and Dr R S Sharma at ICMR in order to discuss the ART regulations. This was attended by Col. Pankaj Talwar, Sec Gen. IfS and Dr Sonia Malik. The proposed changes in the ICMR registration form were discussed. It was also proposed to intensify efforts for the implementation of the ART bill.
3. Attended a meeting on Surrogacy jointly convened by Ob GynDeptt. Medical College Rohtak and Haryana Women's Commission. The IFS view point on this issue was strongly put forth.
4. IFS also participated in the Central Govt. Skill Development programme for ART convened by Dr S N Basu. Members included were Col. Pankaj Talwar, Dr Sonia Malik, Dr Gaurav Majumdar.
5. Attempt are on going to join the Federation of International Gynaec Endocrinology Societies, Italy. This would give the members free access to the website, journal and conference lectures. It offers the members a concessional fees at the annual conference.

Proposed activities for 2019:

1. Meeting on Solutions to Medicolegal problems in ART in conjuction with Delhi Medical Council, MCI and the Consumer and Redressal Court.
2. A meeting with the Women's council of India on Surrogacy and Third Party Reproduction.
3. Continue efforts in regulating ART at ICMR, PNDT deptt.

DR UMESH N JINDAL
Convenor
Research Committee, IFS
Executive Advisor, IFS

FROM THE DESK
RESEARCH COMMITTEE

Indian Fertility Society Net-work for Collaborative studies on Assisted Reproduction Technology (IFSNET)

Introduction

According to a recent report, India faces a high burden of infertility, with 22 to 33 million couples in the reproductive age suffering from infertility. There are distinct socio-religious, economic, legal and political issues related to infertility management specific to the country. Some of the causesof infertility are also different. For example, almost 10-20% of them (or about 5 million) can be attributed to pelvic tuberculosis which is not so common in the Western countries. The problem is similar in several other developing countries.

Unfortunately, there is limited published data from this country posing a great limitation on improving the approach and outcomes of various management techniques, particularly with reference to Assisted Reproduction Technology (ART). It is therefore proposed to establish an Indian Net-work for collaboration for studies on infertility and assisted reproduction technology under the auspices of the Indian Fertility Society.

Aims and Objectives

The primary aim of the Net-work is to establish a group of investigators and other clinicians interested in doing observational/ analytic and experimental research on different aspects of infertility. The Net-work will encourage such undertakings and provide assistance as required.Each investigator/ group of investigators will be free to undertake projects of her/ their interest and seek grants from different agencies.
Some of the objectives can be listed as under:

1. Help in critically analyzing the project and provide suggestions/ consultations
2. Help to find and join collaborators
3. Provide assistance in Research-training programmes
4. Help with ethical issues as appropriate
5. Help with clinical statistical suggestions and analyses
6. Undertake projects at the Net-work level with involvement of interested members
7. Any other assistance as considered feasible and appropriate

Net-work structure

Net-work will comprise of IFS members who are interested in participating and sharing data in one or the other study depending upon their interest. Sharing data does not imply its use by the Net-work unless previously agreed as per the terms of a project. Each project will have its own lead investigator, co-investigators, protocol, terms & conditions, methodology and budgetary provision. The Net-work will not undertake any responsibility for the investigator's project beyond what is specified in the approved project plan. However, the Network will support the project planning, performance and completion.

It is proposed to fix the initial tenure of the Net-work Administrator to a minimum of five years to consolidate the structure and make it viable.
The network will work in association with the research committee of IFS

Net-work administration

Chief coordinator, Sr Research scientist, Statistician

Collaborating centers

Centers who are willing to share data
Who are ready to do part funding
Every center will have to designate an research associate and data operator

Data collection

An online cloud based system of data collection to be developed similar to SART data. The system will ensure the confidentiality and correctness of data. In the long term this network and database will provide infrastructure with the help of which other collaborative projects can be undertaken.

Project budges

Initial st up of network will be funded in part by collaborative centers and IFS .Each project submitted by any member is required to be funded by one or the other funding agency including IFS, Pharmaceutical or other companies and/ or other bodies. The projects will have their own budgets. Every
Project should specify the assistance required from the Net-work including the appropriate payment to the Net-work for that assistance.

IFS PATHSALA - Certified Master Courses

In its endeavor to spread knowledge in the field of fertility, IFS organized two editions of IFS Pathsala -Certified Master Courses in year 2018-2019.

Master courses were uniquely designed with very precise and specific modules covering concepts and latest advancements alongside state of ART laboratory techniques and procedures. Due to excellentcourse content, Experienced faculty, and effective management, master courses was well received and in fact organizers have to increase minimum limit of participants per session.

Master courses also put lot of effort to bring in very heterogenous mix of participants with experience and established practitioners along with young enthusiasts so that participants can tap in to each other experience along with the knowledge shared by faculty. It also had clinicians and embryologists synchronizing among each other.

Master courses in its holistic approach covered "Triad" of Concepts, Hands on laboratory techniques and Standard operating procedures. Experienced faculty with national repute shared their experiences in the field of ovulation induction, reproductive endocrinology and applied genetics. Master courses also witnessed hands on laboratory procedures like semen analysis, IUI setup, comprehensive advanced andrology techniques, cryopreservation of semen, oocytes, embryos and Concepts of embryo culture , media and labware. Master courses also detailed QA/QC (Quality Assurance and Quality Control) measures along with ICMR guidelines for ART Centre.

IFS Pathsala with its first edition laid foundation for future of training in field of fertility with extremely encouraging and satisfying feedback, many enquiries are already flowing in for next and bigger version of IFS Pathsala.

IFS E-PATHSALA
IFS - Reaching Every Corner of the Nation

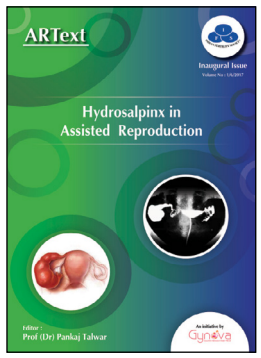
DR GOURI DEVI
President, IFS

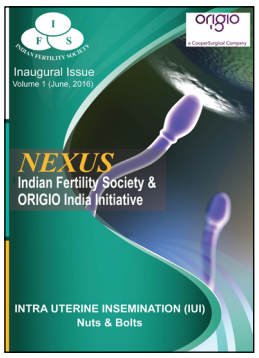
DR PANKAJ TALWAR
Secretary General , IFS

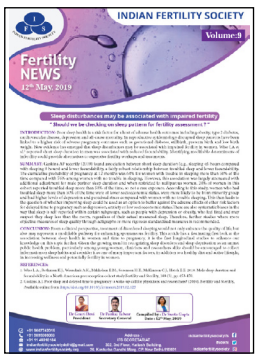
ART TEXT : this has been brought out on various topics like hydrosalpinx , Poor ovarian reserve, adenomyosis and thin endometrium. This was an initiative by Prof Pankaj Talwar who is the chief editor .

NEXUS: An embryology update brought out by Indian fertility society on topics like Semenanalysis, Intrauterine insemination, Semen freezing, sperm function test, media, vitrification, oocyte retrieval and embryo Transfer . This was an initiative by Prof Pankaj Talwar who is the chief editor.
New editions onco navi

DR PANKAJ TALWAR
Chief Editor

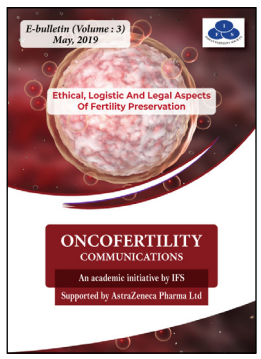




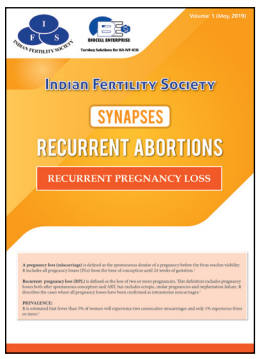


FERTILITY NEWS

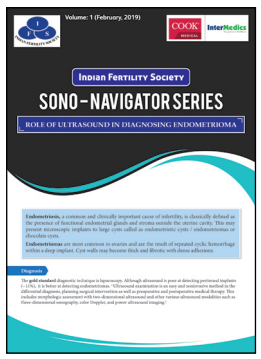
CATALYST



ONCOFERTILITY



SYNAPSES



SONONAVIGATOR

Compiled by
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Fertility Science and Research Journal – An IFS Publication…

Fertility Science and Research, a publication of Indian Fertility Society, is a peer-review journal with triannual print on demand compilation of issues published. The journal's full text is available online at http://www.fertilityscienceresearch.org. The journal allows free access (Open Access) to its contents and permits authors to self-archive final accepted version of the articles on any OAI-compliant institutional / subject-based repository. The journal does not charge for submission, processing or publication of manuscripts and even for color reproduction of photographs.

We are circulating an approximate of 2500 copies. Initially frequency of publication was biannual. Now it has been made triannual.

The Current Issue ……. The current issue deals with interesting and pertinent issues faced by the current day ART specialists. Stem-cell therapy, although still in its nascent stage, has come out with certain options in the management of male as well as female infertility. The subsequent articles deal with the extremely important and burning issue of ovarian reserve and its testing and a study of poor responders and comparison of their managements in the diagnosis as well as the management of infertile couples. Another retrospective analysis of the antagonist cycles to assess the ovarian reserve parameters gives an overall view of the clinical parameters assessing the success of in vitro fertilization (IVF) cycles. An interesting analysis correlates the interleukin concentrations in the follicular fluid states it to be a reliable predictive marker of successful IVF/ outcome. Comparison of fresh versus frozen embryo transfer in IVF cycles highlights the utility of frozen embryo transfer cycles in polycystic Ovarian syndrome (PCOS) and hyperstimulated patients, with comparable efficacy. An article clearly specifies the use of single versus double IUI in ovulation induction cycles. This issue has been nicely brought out the importance of mental and psychological health of patients undergoing treatment of infertility.

Articles can be submitted online
http://www.fertilityscienceresearch.org

DR GOURI DEVI
President, IFS

DR PANKAJ TALWAR
Secretary General , IFS

Dear Dr's,
We are happy to announce a masterclass on the various aspects of Total Laparoscopic Hysterectomy (TLH) and its management with one of the top experts in the field. Get an opportunity to engage in active discussions with the faculty to help in your current practice.

Webcast link for your event
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Saturday
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Topics To Be Covered

1. Tips & techniques for use of Energy during skeletonization of Uterine artery
2. TLH with adhesions/previous cesarean
3. TLH for big size uterus/Multiple Myoma
4. TLH for Severe endometriosis
5. Diagnosis and Management of Bladder and ureteric Injuries
6. How to establish your practice in TLH

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Convenor SIG Endoscopy
IFS 2018-2020

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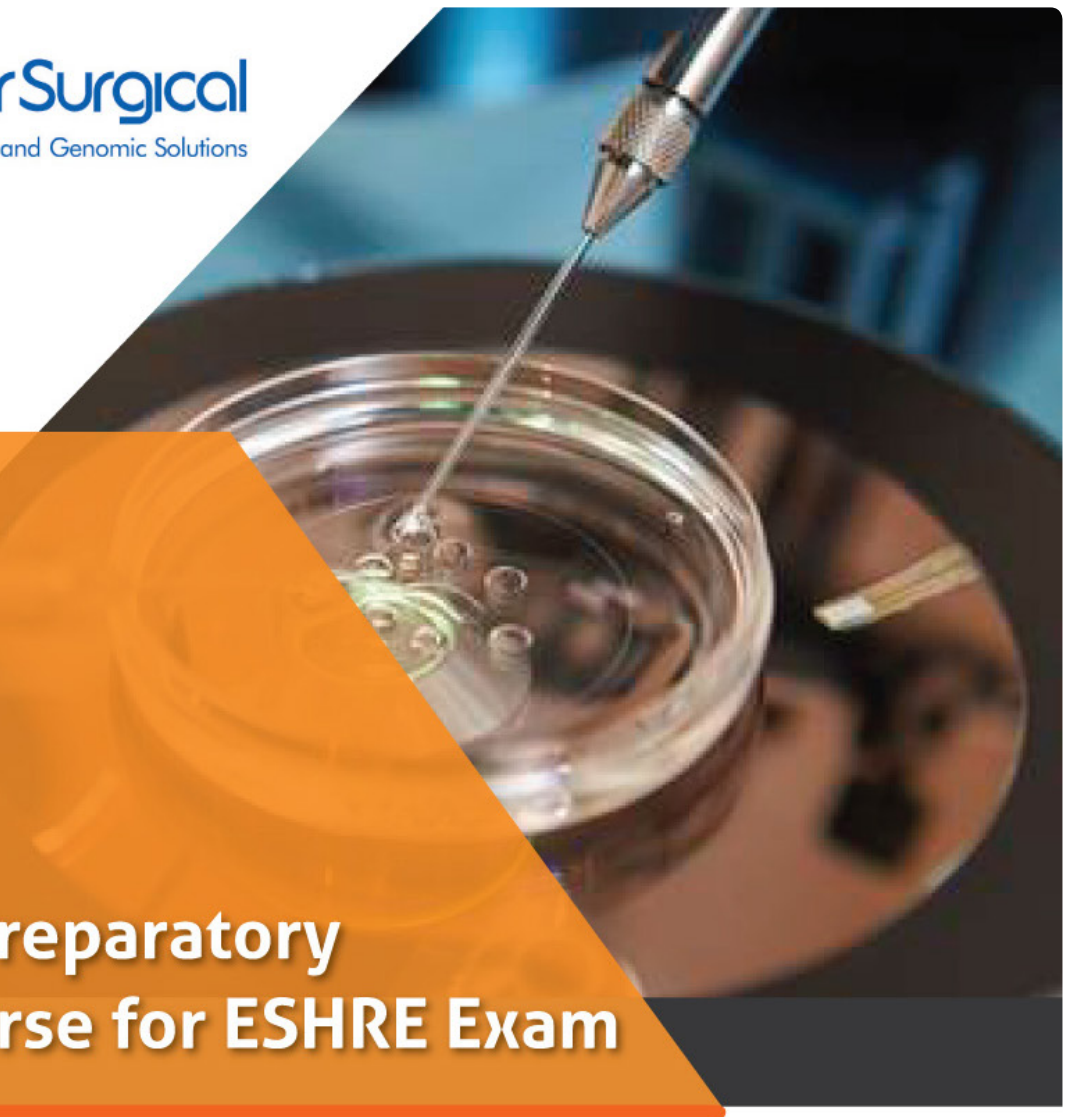

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www.indianfertilitysociety.org

Eligibility:

- MBBS/Post graduate or MSc/PhD in Life Sciences.
- Experience of three years working at an IVF laboratory.

President **Dr. Gouri Devi**
Secretary General **Dr. Pankaj Talwar**
Course Chairerson **Dr. Kuldeep Jain**
Course Director **Dr. Jayant Mehta** **Dr. Arne Sunde**

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Account No. : 50562010067180 | IFSC code : ORBC0100179
Bank Name : Oriental Bank of Commerce | Branch : Connaught Place, New Delhi-110001
please draw your cheques / DD in favour of **"Indian Fertility Society"** payable at Delhi

For Further Information Contact :
Dr. Pankaj Talwar - Secretary General

IFS SECRETARIAT - 302, 3rd Floor, Kailash Building, 26, Kasturba Gandhi Marg,
C.P. New Delhi - 110001 Tel: +91 9899308083, 9810790063, 9667742015 (whatsapp)
E-mail: indianfertilitysocietydelhi@gmail.com Web: www.indianfertilitysociety.org

indianfertilitysociety indianfertilitysociety ifsdelhi

Congratulations to all the candidates successfully passing the Examination DCR & DCE 2018-2019

DCR			
NAME	CENTER	NAME	CENTER
Ms Shrotri Tejashri Murlidhar	SGRH	Ms Niti Vijay	Ridge IVF
Ms Nikita Jindal	SGRH	Ms Deepmala	KJIVF
Ms Renu Lamba	Southend	Ms Jyoti Gupta	KJIVF
Ms Aneesha Minocha	Southend	Ms Indrani Ghosh	Guwahati
Ms Divya Lakshmi A	Jindal	Ms Rachita Chawla	Kochi, Kerala
Ms Princy Mittal	Akanksha IVF	Ms Simmi Arora	Jodhpur
Ms Ruchi Chhabra	Pune	Ms Manvi Tyagi	Ahmedabad
Ms Zeepee Godha	Akanksha IVF	Ms Shilpa Singhal	Primus
Ms Soumya Dash	Mother & Child		

DCE	
NAME	CENTER
Ms Charu Goel	Jindal
Ms Nupur Ahuja	Primus
Mr Shivam Malhotra	SGRH
Ms Andleeb Rubab Shuaib	Southend IVF
Ms Swati Mishra	Akanksha IVF

IFS - Representing India At Global Level

The Joint session of IFS / ISAR was conducted at IFFS world congress Held in Shanghai from 11th - 13th April, 2019

3 panels on improving ART outcome - clinical and embryology perspective and Recurrent implantation failure were held which were highly appreciated and well attended

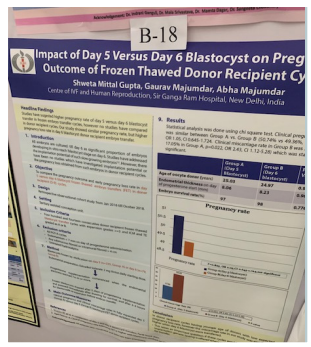
Akanksha IVF Centre team lead by DR. K.D. Nayar

Oral Presentations : International

1. Oral presentation : Role of recombinant Luteinizing hormone as adjuvants to antagonist protocol in poor responders - *Kanad Dev Nayar, Minal Singh, Monica Gupta, Gaurav Kant, Divya Nayar, Shweta Gupta*
2. Trigger Day Progesterone level ã: A guide towards Fresh or frozen transfer and clinical outcome - Shweta Gupta, K D Nayar

Oral presentation / poster presentation (National)

Impact of day 5 vs day 6 blastocyst on pregnancy outcome of frozen thawed donor recipient cycle. Shweta Mittal Gupta, Gaurav Majumdar. 15th May 2019. Sir ganga Ram Hospital research day



Deep Condolence

Indian fertility society expresses grief and sorrow for Dr. Kumud Pasricha who left us for heavenly abode in May 2019. She was the past secretary of Punjab chapter of IFS. She was a remarkable and humble soul, doctor par excellence and deeply spiritual human being. She was full of grit and energy and fought her illness bravely.She was conferred life time achievement award in Dec,2018 at Kochy. May her soul rest in peace. She will always be remembered. Heartfelt condolences.

CHAPTER ACTIVITIES

CMEs on "Recent Advances in ART " were conducted in Kolkata and Chennai on 21st February and 21st March

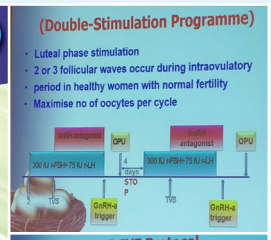
Under the banner of IFS, two out of three CMEs on "Recent Advances in ART " were conducted in Kolkata and Chennai on 21st February and 21st March respectively.

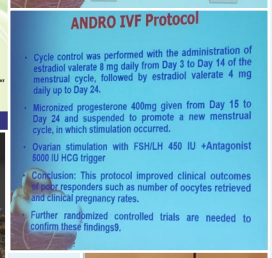
The focus of the meetings was not only to make the delegates aware about the recent developments in the field of assisted reproduction but also teach them how to evaluate and imbibe the latest techniques in their clinical practice.

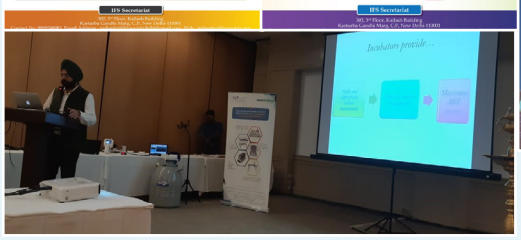
A series of lectures were conducted on the important developments in ART such as newer drugs in ovarian stimulation & endometrial preparation as well as technical advances such as preimplantation genetic screening, witnessing systems, microfluidics and robotic ICSI. Renowned experts in the field of ART presented these lectures. In the end, there was a panel discussion on how to incorporate these techniques in ourroutine clinical practice.All presentations were followed by active discussions.

The meetings were well attended at both the venues (35 plus delegates in Kolkata and 52 delegates in Chennai). Top ART dignitaries such as Dr. Joydeb Roychowdhary (Dean, ESI Medical College, Kolkata), Dr. Ratna Chattopadhyay &Dr. Bani Mitraattended the meeting in Kolkata &Dr. Neeta Singh (Professor, AIIMS), Dr. Priya Selvaraj and Dr. Sujatha Ramakrishnan attended the meeting in Chennai.

We made 4 new members in Kolkata and 2 new members in Chennai.







CHENNAI CME – Recent Advances in ART 17mar2019
Orgnised by : Dr. Gopinath and Dr. Hema

Big thank you to IFS, the faculties _Dr. Sarabpreet Singh, Dr.Bindu Chimote, Dr. Neeta Singh...
Wonderful speech, shared lot of up-to-date information

KOLKATA CME 17th FEB2019

Dr. B.N. Chakraborty could not come because he is not keeping well. Madam Chakraborty came for d inauguration.

Dr Joydeep came as guest of honor

Karnataka chapter on 19th May, 2019 at Hotel La Marvella, Bengaluru

CME on 'Setting up an ART Lab/Clinic' conducted on 19.05.2019. It was a well attended and appreciated CME with a delegate strength of 64. A total of 50 handbooks were handed over to the delegates. A total of 11 new members got registered for Life time membership.

Kerala Chapter - 19th May, 2019 at Kochi

Inaugurating the CME on Enviroment and Reproduction in ART on 19th May, 2019 in Kochi. Moderated a Panel also along with Gaurav Kant which generated lots of interactions from the delegates.

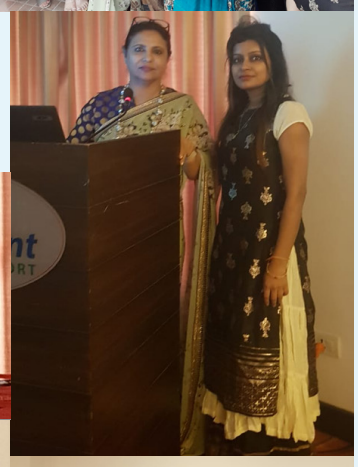
IFS Nepal Chapter at Pokhara on 29th March, 2019

IFS Nepal Chapter hosted their Annual CME at Pokhara on 29th March 2019. IFS were represented by the treasures Dr. Neena Malhotra prof. AIIMS & Dr. Rita Bakshi – Patron of the IFS Chapter Nepal.

Pokhara has around 50 gynecologists and we are glad to inform our turned out was around 50 with a few doctors from Kathmandu, Butwal and Biratnagar also. In fact according to Pokhara doctors it was a rare day with nearly all doctors except a few on Call/ Duty not attending.

INAUGARATION was done by

- Prof. Ashma Rana – Head SAFOG
- Prof. Chandrika – Head of Pokhra Obs & Gyne Society
- Dr. Uma Srivastava – Secretary IFS chapter Nepal
- Dr. Girdhari – joint secretary IFS chapter Nepal
- Dr. Neena Malhotra & Dr. Rita Bakshi



8 out of 50 people became IFS members there itself and also paid up.

- Dr. Niraj Dubey
- Dr. Pradip Shrivastav
- Dr. Laxmi Sunar
- Dr. Aashika Shrestha
- Dr. Rajesh Adhikari
- Dr. Nutan Sharma
- Dr. Dhana Laxmi Gurung
- Dr. Sangita Chakraborty

CHAPTER ACTIVITIES

CME of IFS Haryana chapter organised on 10th Feb 2019 at REWARI

IFS Haryana chapter conducted fifth meeting of calendar year on 10th February at Golden Huts Resorts, Rewari.

This fertility update well attended by more than 60 delegates. Update started with comprehensive talk by Dr Sohani Verma on " Recurrent abortions ". Ouite Interactive Panel on Endometriosis & infertility moderated by Dr shweta Mittal&Dr. NeeruThakral. Dr umesh jindal from Chandigarh gave Fantastic talk on "Endometrial Receptivity ". Lastly panel on Male infertily by Dr pankaj Talwar. He left no stone unturned in Demystifying Male infertility. Thanks to team IFS Dr Gauri ma'm / Drpankajsir, all expert panelist, chaipersons, ROGS Society& all delegates for making the update and knowledge sharingsuccesful. Meeting was well covered by Press coverage like - Amar Ujala, Danik Bhasker, Danik Jagran. The academic activity was well organized & appreciated by all delegates.

19th May, 2019 at Hotel Leela Ambience

IFS Haryana chapter first annual conference superbly arranged on 19 th May at hotel leela ambience under expert guidance of national president Dr gauri and secretory General Dr pankaj. Organising chairperson was Dr Neeru Thakral and co chairperson dr shalu Gupta. Well attended by more than 350 infertility specialist and Gynaecologist from delhi NCR with two workshops and free paper sessions . Conference was inaugurated by DGHS Dr Satish aggarwal and HOD PGI chandigarh dr Smiti nanda and CMO dr Rajora. Academic content is the back bone of any conference and It was a Academic bonanza with wonderful sessions, enlightening talks ,Interactive panels, Role pay, key note address,debates, mesmerising president Oration with participation of almost all national faculty along with international speaker Mr Jose miravet from Spain to make it rich and satisfying experience for the delegates. It was an honour to have all stalwarts under one roof imparting the pearls of knowledge and wisdom. Entire hall was spell bound till End. It was nicely arranged and executed event, appreciated by one and all.

CME "challenges in infertility" was conducted on 18th July 2018 at Gurgaon

We had wonderful national faculty Dr. Alka Kriplani, Dr. Sonia Malik, Dr. K.D. Nayar, Dr. Pankaj Talwar (Secreatary IFS) along with Dr. Bharti Dhorepatil from Pune. The CME was attended by 98 Gynecologists and fertility specialist.

Mesmerising talk on Adenomyosis was given by chief guest Dr. Alka Kriplani Mam. Very informative talk on "Demystifying Semen analysis deliverd by Dr. Pankaj Talwar & wonderful interactive panel by Dr. Bharti Dhorepatil & Dr.Neeru Thakral on" Recurrent implantation failure with expertpanelist from all over Delhi and NCR.

Vision of IFS shared by Dr. Sonia Malik and Dr. Pankaj Talwar. Haryana Chapter vision shared by Dr.Neeru Thakral. Talks and panel were well appreciated by all

CME "Updates in Infertility " was conducted on 12th August, 2018 at ROHTAK

It was attended by 93 gynecologists and infertility specialists from Rohtak and 8 nearby districts.The entire hall was spell bound by Dr Sonia Malik's talk on most simple yet most confusing topic " Tuberculosis and infertility "Wonderful panel discussions were conducted on "Ovulation Induction" by Dr Neeru Thakral and Dr Shalu Gupta and "Endometriosis and infertility " by Dr Shweta Mittal Gupta and Dr Veenu Kadian with other stalwarts of infertility like Dr KD Nayyar , Dr Sandeep Talwar and Dr Smiti nanda HOD PGI medical college Rohtak & dr Mahendroo HOD Khanpur Medical college, being part of panel discussions. Another excellent talk on "Assisted Laser Hatching " by Mr Ram Prakash kept the participants engaged till the end. This academic feast was appreciated by one and all

"Setting up an ART unit " CME at Manesar on 28th October 2018

"Setting up an ART unit" CME at MANESAR on 28th October, post karvachauth day was well attended. Almost 71 participants from all over Haryana and Delhi NCR attended the CME. This CME is part of all India initiative undertaken by Indian fertility Society and partnered by Vardhman Medicare. Dr Gouri Devi & Dr Pankaj Talwar are the guiding force and mastermind behind it.

Audience actively participated in discussions and had great interaction with speakers. Recent ICMR guidelines, difference between guidelines and law, do's and dont's among gynaecologist were few points discussed in details.

The CME covered all aspects of ART lab from setting to trouble shooting and was well appreciated by all for being precise, to the point and with take home messages.

CME of IFS Haryana chapter of organised on 14th Nov 2018 at FARIDABAD

The CME focussed on "Infertility Solutions for a Gynecologist". The academic session started with a talk by Dr Sudha Prasad on " Managing infertility – A Road Map ." The talk received a loud applause from the audience as well as chairpersons. It was a comprehensive overview of infertility management.

The last topic was an interesting panel discussion on " Ovulation Induction: How can we improve our results ?" moderated by Dr Neeru Thakral and Dr Astha Chakravarty. The panellists were eminent Gynecologist and fertility specialists from Faridabad and Gurgaon. Common case scenarios pertaining to infertility were discussed and the audience actively participate in the discussion.

The CMS was attended by 53 Gynecologist and 2 new members were added to the IFS family. The academic activity was very much appreciated by the audience.

IFS Rajasthan Chapter at Hilton

A very interactive and well attended CME organised under the banner of Indian Fertility Society Rajasthan chapter today, on 'Updates on Ovulation Induction'. About 100 delegates participated and got benefitted. Special thanks to our guest faculty Dr K D Nayar Sir and Dr Neeru Thakral Madam for coming all the way from Delhi and Gurgaon to share their experience and knowledge with us.

IFS Mumbai chapter on 10th February, 2019

Environment effects various aspects of health including reproductive health. There is enough robust evidence suggesting linking of toxic environmental agents to reproductive and developmental health outcomes. Reducing exposure to toxins especially in pre-conception and pre-natal period is important, as it may have profound and lasting effects. Healthcare providers should provide guidance and should act to find better alternatives. These focussed meetings have been designed to address the above felt need of environment awareness and its effect on reproduction and ART. Thanks to whole team for their constant support to help us and organize these meetings. Centrally Dr Gauri, Dr Pankaj Talwar and Gaurav Kant for their valuable contributions, without which this initiative would have been not possible. Sincere thanks to local coordinators Dr RajanVaidya(Mumbai), Dr Kunjimoidee (Kochi), Dr Roya Rozati (Telangana) who had been very supportive in this educational initiative. Last not the least, sincere thanks to Mr DilipPatil from Trivector in bringing the program to fruition.

First of these focussed meetings was done at Mumbai on 10th Feb. 2019. Local coordinator was Dr RajanVaidya. It was graced by eminent speakers Dr Firuza Parikh, Dr Chaitanya Nagori, Dr Chimote, Mr Dilip Patil and more than 50 delegates were present. Centrally it was represented by Dr SandeepTalwar and Dr Sweta Gupta. It was well appreciated by everyone and had interesting brainstorming discussions.

Fertivision 2018 - Bringing The Globe Together

14th National conference of Indian Fertility Society

14th, 15th and 16th December, 2018 | Le Meridien, Kochi
Organized by IFS, Kerala Chapter

Fertivision 2018 Report

The 14th Annual Congress of Indian Fertility society was organized at Hotel Le Meridian, Kochi on 14th,15th and 16th of December 2018. This was the first time ever, the prestigious Fertivision was held in South India. The meeting was hosted by the Kerala Chapter of IFS. The organsing committee was headed btDr M Gouri Devi as Chairperson and Dr Pankaj Talwar and Dr K U Kunjimoideen were the organizing secretaries. The past presidents of the IFS were the patrons.

The scientific program was crafted with a theme of 'Beyond all limits.. breakthrough to excellence'. There were 26 international faculty from across the world and 350 national faculty. The conference was attended by 1096 national delegates and 300 plus international delegates. Fertivision 2018 had many 'FIRST' in its cap – Fist ever Fertivision happened in South India, First Fertivision with 26 international faculty, First Fertivision with more than 300 international delegates, First Fertivision which was organized as 'Go Green' conference, First Fertivision with a jam packed workshop on a house boat, First Fertivision with joint sessions with ISAR and ACE etc.

There were 7 pre-congress workshops and each were held in halls fully occupied by the enthusiuastic delegates. The workshops were IFS-IFFS workshop on 'Ovarian Stimulation -Do's and Don't's; Evidence based infertility practice, Reproductive Surgery, Andrology and Semenology, Technology Update, Ultrasonographic imaging in Infertility, IFS-Ace workshop on Technical challenges in Day to day Embryology practice and Andrology &Semenology. The Evidence based fertility practice workshop was held onboard a house boat sailing on the backwaters of Kochi. The IFFS workshop was led by Prof Paul Deveroy (Belgium) and Prof Basil Tarlatzis (Spain).

The conference was inaugurated on 14th evening by the Vice chancellor of Kerala Health university Prof MKC Nair. DrGouri Devi, The President IFS presided over the meeting. Dr Pankaj Talwar, Dr Kunjimoideen, Dr Sudha Prasad and Dr KD Nayar spoke during the inaugural session. The inauguration was followed by 'Keraleeyam' a unique show casting of Kerala's cultural dance performance by the eminent artists from Kerala Kalamandalam. There were two plenary lectures immediately before the inauguration. One was about the legal hurdles for a practicing fertility specialist by Dr Hitesh Bhat and the other about 'Ruminations of a restles retiree' by Dr Gita Arjun. The Fertivision 2018- Embryology oration was awarded to Prof Arne Sunde, from Norway.

There were two orations on 15th December 2018, ie on the second day. The president orations was on 'Gazing at the horizon' done by Dr M Gouri Devi, The President IFS. The Fertivision 2018 Oration on Clinical Reproductive Medicine was awarded to Prof William Ledger (Australia), who spoke on 'Ovarian biomarkers- Changing Trends'.

Dr Sudha Prasad was awarded with 'President elect oration' and she delivered a lecture on 'Red flags in Infertility treatment'.

The joint session with ISAR was led by DrRishmaPai (President ISAR) and Dr Krishnakumar (Secretary, ISAR). The other prominent Plenary sessions were 'Does endometrial thickness really matter?' by Prof JLH Evers (Netherlands) and 'Role of Freeze all in contemporary ART Practice' by Prof Basil Tarlatzis (Spain). There were well attended lectures by BalaBagavath(USA), Ben Mol (Australia), Carmen Morales(Spain), E Balaji (Singapore), Jayant Mehta (UK), Jayaprakasan K (UK), Nikolaos Polyzos (Spain), Osama Shawki (Egypt), Sesh Kamal Sunkara (UK), Samuel Ribeiro (Portugal), Stuart Long (UK) and Yacoub Khalaf (UK). The widest arena of international speakers and the international delgates from SAARC countries, Middle eat and African countries were the sparkling highlights.

Organised by

IFS
INDIAN FERTILITY SOCIETY

15th Annual Congress of Indian Fertility Society

FERTIVISION 2019

6-8 December

The Leela Ambience Hotel, Gurugram
New Delhi | India

Theme: Beyond Tomorrow

www.fertivision2019.com

Invitation

Welcome to *FERTIVISION 2019*

Dr. M Gouri Devi
Organizing Chairperson
FERTIVISION 2019

Dr. Pankaj Talwar
Organizing Secretary
FERTIVISION 2019

Dear Friends,

On behalf of the Indian Fertility Society (IFS), we are extremely pleased to announce and cordially invite you to the much awaited academic event – the **15th National Annual Conference - Fertivision 2019**, to be held on **6th, 7th & 8th December 2019** at Hotel **The Leela Ambience, Gurugram, New Delhi / NCR, India**.

This conference is aimed to provide the most comprehensive academic platform in the field of Infertility and Assisted Reproductive Technology (ART)" befitting the theme of the meeting "Beyond Tomorrow"

Renowned and leading expert faculty from around the world would gather and deliver talks in our cutting edge scientific program which will not only enrich your current knowledge and clear all doubts faced in day-to-day clinical practice, but will also enlighten you about the latest innovations and ongoing research.

A large number of renowned international faculties have already confirmed their participations till date. The pre-congress workshops on 6th December are specially designed for informal in-depth training with hands on sessions on simulators and live, where ever feasible. There will be 4 simultaneous running streams on 7th & 8th December covering a wide variety of topics, enabling you to choose the deliberations specific to your area of interest and clinical practice. We are having a dedicated hall for the esteemed embryologist friends.

The best oral and poster presenters under various categories and the quiz winners will be honored with special awards and prizes. Do join us in large numbers and update your knowledge with most updated current standards in clinical practice, as well as get inspired to innovate further to overcome remaining enigmatic issues!

The three days of scientific program will encompass didactic lectures, keynote presentations, panel discussions and orations. There will be 9 Pre-conference workshops based on Ovulation Induction, Ultrasound, Andrology, Embryology, Hands on Embryo Transfer, Ovum Pickup and PGS and more. These workshops will be in addition to the special state of the art workshops by the faculty from IFFS and ESHRE. We expect delegates across India, Sri lanka, Bangladesh, Nepal, Middle - East Countries and African Nations and the arrangements are being made to accommodate more than 2500 delegates.

The exhibition area will be one of the highlights of the conference. Exhibiting provides tremendous benefits to both participating industry and the society. Tea, coffee and lunch will be served confluent with the trade area to allow optimal interaction between the trade companies and delegates during beverage and lunch breaks.

We invite you to participate in the Fertivision 2019 and exchange your expertise with more than 2500 specialists in the field of Assisted Reproduction.

We look forward to your active participation and suggestions for successful conduct of the conference.

With Our Best Regards

and All Executive Committee of Current IFS team

15th Annual Congress of Indian Fertility Society

FERTIVISION 2019

6-8 December The Leela Ambience Hotel Gurugram, New Delhi, NCR | India

Organised by IFS Indian Fertility Society

Registration Form

Title Prof/ Dr/ Mr/ Ms _____ Gender : Male ☐ Female ☐

First Name _____ Last Name _____

Institution _____ IFS Member No. _____

Correspondence Address _____

_____

City _____ Pin Code _____ State _____

Mobile No. _____ Email _____

(All the above fields are mandatory)

Limited Seats

Choose from 10 Pre Conference Workshops | 6 December — Choose Any 1 Workshop

1)	☐ *IFFS Workshop on Do's and Don'ts in Ovarian Stimulation*	7)	☐ *QA / QC*
2)	☐ *Reproductive Surgery*		***Pre Lunch Workshop (0900 - 1300 Hrs)***
3)	☐ *Ultrasonography Imaging In Infertility*	8 A)	☐ *Counselling & Psychological Support*
4)	☐ *Andrology & Semenology*		***Post Lunch Workshop (1400 - 1700 Hrs)***
5)	☐ *Ovum Pickup and Embryo Transfer (With Simulators)*	8 B)	☐ *Research Methodology*
6)	☐ *Cryobiology*	9)	☐ *PGT and Genomics*

Registration Fees

Inclusive of 18% GST

Please tick the appropriate checkbox

Category	Early Bird Fees Till 15th July 2019	Regular Fees Till 15th October	Onspot
IFS Member	INR 10500 ☐	INR 12500 ☐	INR 14500 ☐
Non IFS Member	INR 12500 ☐	INR 14500 ☐	INR 16500 ☐
Conference Registration plus Life Time IFS Membership	Embryologist INR 14500 ☐ / Gynaecologist INR 15500 ☐	Embryologist INR 16500 ☐ / Gynaecologist INR 17500 ☐	Embryologist INR 18500 ☐ / Gynaecologist INR 19500 ☐
PG Students (No Dinner)	INR 6000 ☐	INR 7000 ☐	INR 8000 ☐
Accompanying Person	INR 10500 ☐	INR 11500 ☐	INR 12500 ☐
Foreign Delegates	$ 350 ☐	$ 400 ☐	$ 500 ☐

Inclusive of 18% GST

Conference Registration Fees Includes

- 18 Hrs of World Class Academic Program with Access to Best & Brightest International & National Faculty
- 3 Lunches and 6 Tea / Coffee Served During the Conference on 6, 7 & 8 December
- Banquet Dinner on 7 December
- Conference Kit (Including Bag, Badge, Notepad, Certificate & Pen)
- 1 Pre Conference Workshop
- Accompanying Person is Entitled for Food Coupons Only

Cancellation Policy

- Cancellation till 31st October, 2019 – 50% Refund.
- Cancellation from 1st November, 2019 – No Refund.
- All refunds will be made after the congress.

Mode of Payment

1. Bank Draft/Cheque - To be made in favor of "INDIAN FERTILITY SOCIETY"

2. Bank Transfer Details

IFS Account Name : Indian Fertility Society
Account Number: 50562010067180
IFSC Code : ORBC0100179
Bank Name: Oriental Bank of Commerce
Branch: Connaught place, New Delhi- 110001

Cheque / Draft No. _____ **Total Amount** _____

Note: Kindly email us bank deposit slip / UTR number once you made the payment for our record. Payment confirmation will take 7-10 working days post deposit of cheque, DD or RTGS

3. To Register online log on to www.fertivision2019.com

Congress Manager's

Mr. Vikas Sharma
Conferences International
B-220/2, 2nd Floor,
Opposite Kali Masjid, Savitri Nagar
New Delhi – 110017
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Email: fertivision2019@gmail.com

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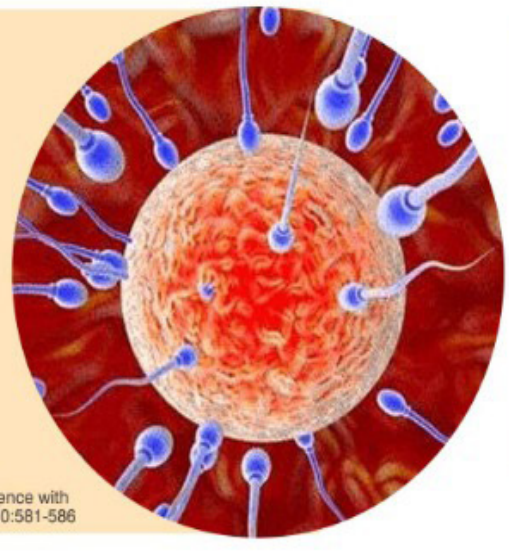
Ref.: Isoyama R. KAWAI S. Shimixu Y et al. Clinical Experience with Methylcobalamin for male infertility. Hinyokika kiye 1984;30:581-586



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Methylcobalamine	500 mcg
Vit C	100 mg
Niacinamide	50 mg
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Vit B2	10 mg
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Folic Acid	1 mg
Vit A	5000 I.U
Vit D3	500 I.U
Vit E	25 I.U
Zinc Oxide	15 mg
Cupric Oxide	2.5 mg
Sodium Selenate	60 mcg
Mangnese Chloride	1.4 mg
Chromium Chloride	65 mcg

In

- Infertile couple
- Male Infertility
- Prostate Cancer
- Pre-eclampsia & IUGR
- Uterine Fibroid Tumours
- Habitual & Spontaneous Abortion

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