2024, Volume 24, July, Issue 03

AOGD BULLETIN

Shared Decision Making - Enhancing Women Emancipation

Theme

Infertility: Challenges Make us Stronger

AOGD SECRETARIAT
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Message from the President

President

Dear AOGDians,

Namaskar

Welcoming this relief in the capital from the scorching summer heat and sweltering temperatures along with the magnificent World cup win by our Men in Blue! They have proven that nothing is above teamwork and ultimately every single individual's contribution matters. Similarly, our association is committed to our theme each month: "Shared Decision Making- Enhancing Women Emancipation" and working relentlessly towards reaching our goal!

We are humbled by the heartfelt appreciation and encouragement that we are receiving for AOGD work and grateful for your enthusiastic participation in all AOGD events. The June issue of the bulletin 'Minimal Access Surgery: Principles and Practices' was very well received among students and teachers alike. The present issue is on Infertility and will focus on current updates in reproductive medicine, taking you through initial evaluation, IVF protocols, and setting up a centre along with an interesting perspective on the surrogacy act and ovarian rejuvenation. With increasing years of infertility and no concrete results, both partners have been shown to even suffer a silent separation, which makes our job as clinicians difficult.

This month AOGD members organized a lot of informative webinars on relevant topics along with the first module of the certificate course of the medico-legal committee. Last month also marked the celebration of International Yoga Day on 21st June where AOGD members practiced the mind and body balancing exercise.

I would like to encourage all residents and colleagues to become members of our prestigious association. We have an active website (www.aogd.org) where you can catch a glimpse of past and future planned activities.

Best wishes and happy reading!

Dr. Ashok Kumar MD, PhD, FICMCH, FICOG, FAMS
President, AOGD
Vice Chairperson, Elect, ICOG, an Academic Wing of FOGSI
National Corresponding Editor, Journal of Obstetrics & Gynaecology of India
Director Professor & Head
Department of Obstetrics & Gynecology,
Atal Bihari Vajpayee Institute of Medical Sciences &
Dr. Ram Manohar Lohia Hospital, New Delhi

Message from the Hon. Secretary

Hon. Secretary

Dear AOGD Members,

Warm wishes from the AOGD secretariat at ABVIMS & Dr. RML Hospital.

As we approach the end of the first quarter of this annual tenure, it's heartwarming to receive so much warmth and affection. The current issue focuses on some of the most relevant topics on infertility. The editorial team is putting immense effort into delivering the best. We hope it is keeping up with your expectations.

The previous month had some wonderful offline as well as online programs despite harsh high temperatures. The first module of the certificate course in medicolegal training was successfully conducted on 8th June. International Yoga Day was celebrated with full enthusiasm and vigor on the serene morning of 21st June. AOGD subcommittees are also working hand in hand to continue the journey of skill and knowledge dissipation. The coming month will observe the world population day and an array of activities will be conducted all over Delhi. The much-awaited postgraduate academic fiesta is also scheduled in the current month.

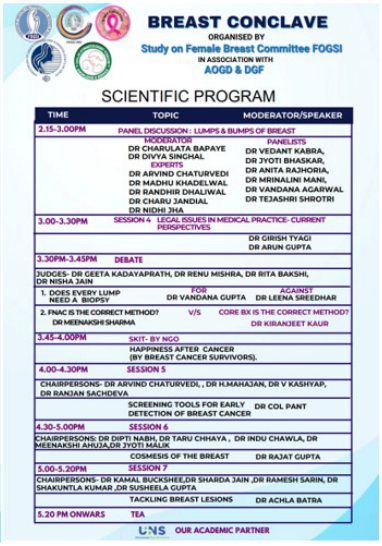
The AOGD annual conference will be held from the 22nd to 24th Nov, 2024. Early bird registration is available only till 31st July. We hope to put up a grand show with the support of every AOGDian.

The victory of the Indian cricket team is a live example of yet another success story of hard work, resilience, and redemption against seemingly unassailable odds. Let's all inspire ourselves to keep marching towards our goal relentlessly. Wishing you all healthy and happy monsoons!

Left to Right: *Dr. Vandana Agarwal, Dr. Neha Pruthi Tandon, Dr. Kamna Dutta and Dr. Geetanjali Nabiyal*

1st June 2024

Breast Conclave organized by Study on Female Breast Committee FOGSI in association with AOGD & DGF



4th June 2024

Webinar by FOGSI MTP Committee, No to VAW Committee & AOGD

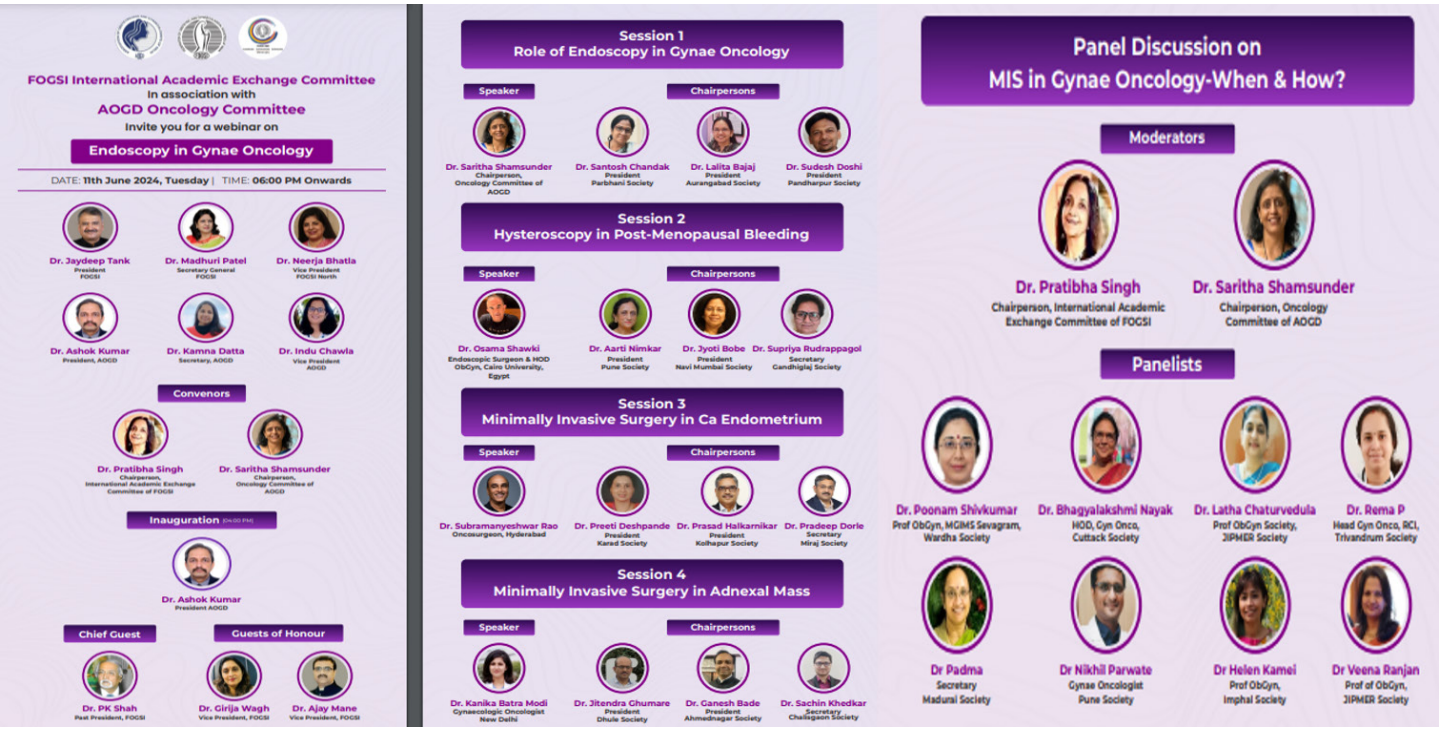
7th June 2024

4th symposium on BEYOND PCOS at Le Meridien, Delhi

8th June 2024
First module of certificate course on Medicolegal training at BLK Hospital – AOGD Medico legal subcommittee

11th June 2024

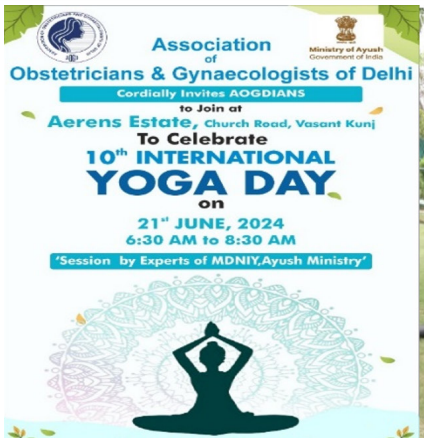
Webinar by AOGD oncology committee & FOGSI International Academic Exchange Committee on Endoscopy in Gynae Oncology



20th June 2024

Webinar on ADOLESCENT PCOS by SIG PCOS IFS in association with Infertility and Endocrinology AOGD Subcommittee & IFS Haryana chapter

21th June 2024: International Yoga Day Celebration



22nd June 2024: Webinar on Caesarean Scar Pregnancy by Endoscopy Subcommittee

Time	Topic	Speaker
6:00 - 6:05 PM	Introduction	Dr. Indu Chawla
6:05 - 6:15 PM	Address by the Chief Guest & Guest of Honour	
Session 1		
Chairpersons: Dr. Reena, Dr. Indu Chawla, Dr. Kanika Chopra, Dr. Neha Varun		
6:15 - 6:35 PM	Caesarean Scar pregnancy (CSP)- What all do we need to know	Dr. Swati Agrawal
6:35 - 6:55 PM	Ultrasound guided management of CSP (Video session)	Dr. Farendra Bhardwaj
6:55 - 7:05 PM	Discussion	
Session 2		
Chairpersons: Dr. Manju Puri, Dr. Alka Sinha, Dr. Aruna Nigam, Dr. Shivani Sabharwal		
7:05 - 7:20 PM	Laparoscopic management of CSP (Video Session)	Dr. Kanika Jain
7:20 - 7:40 PM	Hysteroscopic Management of CSP (Video Session)	Dr. Ajay Aggarwal
7:40 - 7:50 PM	Discussion	
7:50 - 8:00 PM	Vote of Thanks	

Click Here To Register

Meeting Organizer
CONFERENCES INTERNATIONAL

26th June 2024

Webinar- janjagrukta by Community Health & Public Awareness Subcommittee & MTP committee FOGSI

27th June 2024

Webinar on what's new in Endometrial Cancer by AOGD Oncology Subcommittee & Medical Education Committee FOGSI

29th June 2024
CME on Demystifying Endometriosis by AOGD Endometriosis Subcommittee

Department of Obstetrics & Gynaecology, LHMC , New Delhi
in association with
AOGD Endometriosis Committee
Presents
CME on
Demystifying Endometriosis for Budding Gynecologists
Tips and Tricks

Saturday | 29th June, 2024 | 10:00 AM - 1:00 PM | Venue: MEU Hall, LHMC

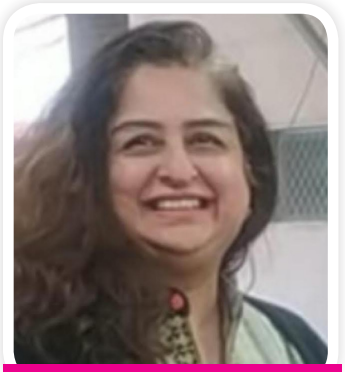
Chief Guest: Dr. Sarita Beri, Director LHMC
Guests of Honour: Dr. Ashok Kumar, President AOGD; Dr. Alka Aggarwal, Ex-Prof LHMC; Dr. Praveen Mittal
Organising Chairperson: Dr. Reena Yadav
Co-Chairperson: Dr. Kanika Jain
HOC: Dr. Apoorva Kulshreshta

Time	Topic	Speaker
10:00 AM - 10:15 AM	Welcome Note & Introduction by Dr Reena Yadav Followed by Small Keynotes by Chief Guest & Guest of Honours	
Session 1		
Chairpersons: Dr. Chandra Mansukhani, Dr. Rashmi Malik, Dr. Payal Chaudhary		
10:15 AM - 10:30 AM	Diagnosing Endometriosis-A visual guide for beginners	Dr. Ratna Biswas
10:30 AM - 10:45 AM	Scar Endometriosis-Tricks to diagnose and manage	Dr. Reena Yadav
10:45 AM - 11:00 AM	Expert Comments	
Session 2		
Chairpersons: Dr. Malvika Sabharwal, Dr. Indu Chawla, Dr. Sharda Patra		
11:00 AM - 11:20 AM	Laparoscopic management of Endometriosis- Video session	Dr. Kanika Jain
11:20 AM - 11:40 AM	Adenomyomectomy & Resection of DE lesions laparoscopicily-video session	Dr. Debasis Dutta
11:40 AM - 11:50 AM	Expert Comments	
Session 3		
Experts: Dr. Abha Majumdar, Dr. Kiran Aggarwal, Dr. Pikee Saxena		
11:50 AM - 12:35 PM	Panel Discussion: Traversing the crossroads of infertility in endometriosis - a case based discussion Panelists: Dr. Garima Kapoor, Dr. Neeti Tiwari, Dr. Divya Pandey, Dr. Shikha Jain, Dr. Kanika Chopra, Dr. Sakshi Nayar	Moderators: Dr. Ruma Satwik, Dr. Swati Agrawal
12:35 PM - 12:45 PM	Expert Comments	
Vote of Thanks		Dr. Apoorva
12:45 PM - 1:30 PM	Lunch	

Forthcoming Events

- 7th July – Postgraduate Academic Fiesta – Miniauditorium, LHMC, 9 am – 5 pm
- 13th July – CME cum workshop on Ovulation induction and IUI – Infertility and Reproductive Endocrinology Subcommittee, LHMC, MEU Hall, 10 am – 1 pm
- 14th July – Symposium - PCOS and metabolism: diagnosis and decision, 7.30 pm onwards
- 24th July – Webinar on GDM, Community Health and Public Awareness Subcommittee – 3.30 – 5 pm
- 25th July – Colposcopy workshop Oncology Subcommittee
- 26th July – Monthly Clinical Meeting – R & R Army Hospital
- 30th July – CME on contraception by ABVIMS

From the Editors Desk



Chief Editor

Monsoon greetings from the Editor's Desk

I hope this edition finds you in the pink of health and heights of spirits in this refreshing change of season. Our majestic World Cup victory is yet another reminder that hard work and consistency eventually pay off. Our team is also working tirelessly in bringing out each issue with utmost detail and dedication so we are obliged to receive your appreciation. This month we are focussing on Infertility and its challenges.

As we all know, IVF is increasingly being used as a method for conception. Thorough evaluation of every couple is a must, to make sure that a preventive and easily manageable cause is not missed out before proceeding to ART methods. Similarly, male partner evaluation is warranted in every case to avoid unnecessary over-investigation of the female partner. Once the decision for IVF has been finalised, it is crucial to follow a standardized protocol at every center to ensure maximum oocyte yield without the risk of ovarian hyperstimulation and embryo transfer at the correct stage and number. The success of ART procedures is directly proportional to the sanctity of IVF labs hence it is vital to understand quality management systems in creating an optimal environment for the culture of oocytes and embryos.

The new surrogacy act bans commercial surrogacy allowing it only for altruistic reasons, establishes criteria for the surrogate and intended parents, and a regulatory framework for governing the clinics. The implications of this act have received both positive and negative reviews and it must be subjected to periodic checks to ensure the rights of all parties involved are well protected.

We shall be covering all these topics in the current bulletin. My heartfelt gratitude to all the authors for the prompt submission of their exceptional and insightful articles. We look forward to any suggestions and feedback from our readers to help us bring out a better version each time!

Dr. (Prof) Renuka Malik

Editor

Professor and Senior Consultant, ABVIMS & RML Hospital

Editorial Team: (Left To Right) Dr. Kanika, Dr. Preeti, Dr. Renuka, Dr. Kavita. (Second Row Left To Right) Dr. Seema, Dr. Niharika

Thought for the month: Happiness will never come to those who fail to appreciate what they already have –Buddha

Diagnostic Pathways for Investigation of an Infertile Couple

Dr. Kanika Kumari

Senior Specialist, Department of Obstetrics and Gynaecology, ABVIMS and Dr RML Hospital, New Delhi

INTRODUCTION

WHO defines infertility as a disease of the male and female reproductive system that leads to failure to achieve pregnancy after 12 months of regular and unprotected sexual intercourse. The incidence of infertility is 1 in 6 people of reproductive age.[1] In 32% of infertile couples the problem is in females, in 32% problem is in males, in 17% both males and females are responsible and in 19% of couples causes are unexplained.

1. Evaluation and treatment is indicated in:-
2. Women < 35 – 12 months of failed attempts.
3. Women >35yr – 6 months of failed attempts.
4. Women >40yr – immediate evaluation.
5. Women with a condition
6. Oligomenorrhea or amenorrhea
   (a) Known or suspected tubal, uterine, or peritoneal disease.
   (b) Stage 3 or 4 endometriosis
   (c) Known or suspected male infertility.
   (d) Sexual dysfunction.
   (e) Genetic or acquired condition that predisposes to diminished ovarian reserve (like radiation exposure/radiotherapy, chemotherapy, and FMR1 permutation)

   Requires immediate evaluation.[2,3]
7. Single women, women in same-sex relationships, or heterosexual women who may require donor sperm.[3]

Causes of infertility

In 40% of couples, the female partner is either the main or a contributing cause of infertility. In 40% of cases, the male partner is the main causative factor.

In 20% of couples, there are no identifiable reasons, termed as unexplained infertility.[4]

But in 25% of cases, more than one factor is involved.

Diagnostic evaluation of infertile couples includes prepregnancy counseling and evaluation, history, examination, and investigations.

Prepregnancy counseling and evaluation

The WHO advises preconception counseling and care between 3 and 6 months before trying for pregnancy because of its positive impact on maternal and child health outcomes. Prepregnancy counseling is important to optimize the health of females to reduce the adverse effects on the health of women, fetus, and neonates It also helps in identifying the modifiable risk factors so that by correcting them fertility can be improved. We counsel regarding immunization in the prepregnancy period, genetic counseling, screening for Ca Cervix, and infectious diseases.

During this, we take the opportunity to educate women about various ways to maximize fertility like timing and frequency of intercourse.[5] Start an active form of folic acid during this counseling and also educate them regarding the importance of it.

History

Female

The main historical factors to find out from females are the following:-

- Duration of infertility and previous evaluation and treatment.
- Coital frequency and timing.
- Sexual dysfunction.
- Menstrual history: as the age of menarche, cycle interval, and length, characteristics, presence of premenstrual symptoms, onset and severity of dysmenorrhea, and signs of ovulation like LH Kit tests, cervical mucus changes.
- PID, sexually transmitted infections, tuberculosis whether genital or extragenital.

- Previous history of surgery mainly abdominal or pelvic procedures eg. Endometriosis and leiomyomas.
- Contraception and methods.
- Thyroid disorder, galactorrhea, hirsutism, and visual field defect.
- Pelvic or abdominal pain or dyspareunia.
- Cervical cancer screening tests and treatment.
- Current medications or health supplements as they may contain steroids.
- Occupation and exposure to known environmental hazards.
- Use of nicotine products, alcohol recreational drugs, or illicit drugs.
- Dietary and exercise habits.
- Use of gonadotoxic medications and radiotherapy or chemotherapy for any malignancy.
- Previous obstetric history gravida, para, fertility treatment, pregnancy outcome, and delivery route.

Male

Due to the high prevalence of male factors in infertility in infertile couples, a basic medical history and evaluation of male partners is necessary. The purpose of evaluating males is to determine the cause of the male factor, to identify 20% of males who can be normalized with the treatment, and to determine whether ART would benefit the couple.[6]

The following points should be elicited:-

- Sexual dysfunction like erectile or ejaculatory dysfunction.
- Use of excessive smoking and alcohol.
- Prior fertility
- Childhood illness and developmental history.
- Previous surgery for cryptorchidism varicocele or any injury.
- Systemic medical illnesses like diabetes, tuberculosis, autoimmune diseases, liver failure, chronic renal failure, and sickle cell disease.
- Medications used like anabolic steroids and supplements may contain testosterone.
- Medication for allergies or exposure to gonadal toxins like insecticides, and pesticides.
- Malignancy of pituitary, testes, adrenals, and sellar masses their surgical or radiation treatment.
- Anosmia(Kallman syndrome).
- Breast enlargement or galactorrhea.
- Tuberculosis, prostatitis, and sexually transmitted infections can cause vasal scarring and obstructive azoospermia.
- Use of sexual lubricants.

PHYSICAL EXAMINATION

Female

Crucial factors in female physical examination are:[2]

- General physical examination – weight, BMI, vitals, thyroid enlargement, and cervical lymphadenopathy.
- Tanners staging of breast, axillary, and pubic hair.
- Breast for secretions, mass, and their character.
- Skin examination for hirsutism, acanthosis nigricans, acne, and androgenic alopecia to look for signs of androgen excess.
- Abdominal examination for tenderness in the lower abdomen, organ enlargement, or masses.
- Per speculum examination for vaginal or cervical abnormal discharge, polyp.
- Per vaginum examination for uterine size, shape, position, mobility, and tenderness, adnexal masses or tenderness.
- P/V/R examination for rectovaginal mass, tenderness, and nodularity.

Male

The main factors to examine are: [6]

- Body weight and BMI.
- Muscle mass indicates the use of steroids.
- Gynecomastia.
- Secondary sexual characteristics.
- Examination of the penis to look for hypospadias, Peyronie plaques, and phimosis.
- Scrotal examination for testicular size, presence or absence or thickening of vas deferens, epididymal lesions, varicocele, and hydrocele.

Investigation

Female

Laboratory and imaging tests for workup of infertility in females should focus on[2,3]

- Ovulatory function
- Ovarian reserve
- Genital tuberculosis
- Other endocrine systems
- Structural abnormalities.
- Peritoneal factors

Ovulatory dysfunction

It should be suspected in females with a history of oligomenorrhoea or amenorrhoea. However, one-third of females with normal menstrual cycles are anovulatory. So, confirmation of ovulation is a must. The tests for confirmation of ovulation are:-

1. Follicle monitoring

   It can be done by transabdominal sonography or transvaginal sonography but the transvaginal route is preferable. Baseline USG on D2 or D3 of the cycle is to be done to check for remnant follicles or cysts from the previous cycle and whether the endometrium has cleared properly. Then do USG on D9 or D10 onwards every alternate day and measure the size of the follicle till it reaches the size of 16mm followed by daily monitoring is recommended till it ovulates. The dominant follicle is round with smooth borders and hypoechoic. Ovulation occurs on the 14th or 16th day in normal cycles and may be on the 9th or 10th day in shorter cycles and on the 19th or 20th day in longer cycles. The signs of ovulation are:-

   - Sudden disappearance or regression in size of follicle.
   - Irregular margins.
   - Presence of intrafollicular echoes.
   - Free fluid in the pouch of dougles.
   - Increase in perifollicular blood flow velocities on Doppler.

2. Luteal progesterone

   Serum progesterone in the luteal phase provides an objective and reliable measure of ovulation. It should be measured one week before the expected onset of the next menses i.e. on day 21. S. Progesterone >3ng/ml confirms the ovulation.[3]

3. Urinary LH

   Urinary LH testing using "ovulation predictor kits" can detect the midcycle LH surge that precedes ovulation within 1-2 days. It should be performed on midday or evening urine specimens that correlate well with the peak in serum LH. Patients with PCOS have tonic basal LH elevation so in these patients results may be false positive.

Ovarian reserve

It describes reproductive potential as a function of number of oocytes. Ovarian reserve tests should augment and not replace patient counseling based on age and diagnosis. Poor ovarian reserve does not imply an inability to conceive or subfertility. Ovarian reserve tests should be interpreted after taking into account her age, risk factors, prior treatment, and response of the individual patient. The tests for ovarian reserve are: [7]

1. AMH

   It is a granulosa cell-derived hormone of secondary, preantral, and small antral follicles up to 4mm in size. It can be measured at any point of time/day in the menstrual cycle. It remains valid even after ovarian suppression by smoking and oral contraceptives, GnRH agonists, and pregnancy. AMH<1ng/ml indicates poor ovarian reserve.

2. Antral follicle count

   The antral follicle is resting and appears as a small fluid-filled sac that contains an immature egg. It is to be done on Day 3 of the cycle by transvaginal sonography. Basal ovarian volume is also measured along with it. Ovarian volume >10ml is abnormal. Antral follicles are in the 2-10mm size range. They are well-defined anechoic cysts with smooth margins and the absence of internal septations or nodularity. They are measured in each ovary. A cut-off value of 10 in total for both ovaries is taken as normal.[8] It may be a false positive in PCOS females.

3. FSH and Estradiol

   Both are measured on Day 3 (day 2- day 4) with Day 1 being the day of full flow. FSH - >10mIU/ml indicates high levels as per WHO's second international standards and estradiol >60-80pg/ml indicates poor ovarian reserve.

4. Inhibin B

   Its levels are not useful as it is a late finding for diminished ovarian reserve.

Genital tuberculosis

The National Strategic Plan (NSP) for TB elimination 2017-2025 aims for END TB in India. It adopts strategies under four groups DETECT, TREAT, PREVENT, and BUILD.

As per March 2024 report of MOHFW the incidence of TB in India is 27.8 lakh. So, Universal screening of high-risk cases/vulnerable individuals attending hospital private or Government is recommended. 60-80% of females with genital tuberculosis have infertility. So, genital tuberculosis should be ruled out by doing an endometrial biopsy in the premenstrual phase(late secretory phase).

The diagnosis is made by detection of acid-fast bacilli on microscopy or culture on endometrial biopsy tissue or histopathological detection of epitheloid granuloma on biopsy tissue. Tb –PCR may be false positive and alone should not be taken as diagnostic. Testing menstrual blood on Day 2 of the menstrual cycle by instilling and aspirating 10-20cc of normal saline in the vagina or sampling from the cervix using a speculum are alternative methods for taking samples and diagnosing.

Other endocrine systems

1. TSH - it is to be measured if period irregularity is present. Or the symptoms of thyroid disorder present.
2. Prolactin – is to be done in women with galactorrhea or oligomenorrhea.
3. Androgen measures – if signs of androgen excess or oligomenorrhea the serum total and free testosterone, 17 hydroxyprogesterone. If testosterone is >200ng/ml then USG and computed tomography of adrenal glands are to be done to rule out androgen-secreting tumors. If 17 hydroxyprogesterone is >200ng/

dl the perform ACTH stimulation test to exclude 21-hydroxylase deficiency.[3]

Structural abnormalities

Fallopian tubes

1. Hysterosalpingography(HSG) is the procedure used to visualize the uterus and tubes by injecting radiopaque contrast through the cervix during fluoroscopy. It is mainly used for checking the patency of tubes. Proximal and distal tubal occlusion, salpingitis isthmica nodosa, and peritubal adhesions may be seen with HSG. The positive predictive value is 38% and the negative predictive value is 94%. So, the nonpatency of tubes on HSG requires further evaluation by laparoscopy with chromopertubation. It should be done between 7-10 days of the last menstrual period. The dye is injected through the cervix with the help of a catheter, 8-F or 10-F Foley catheter, or Leech Wilkinson HSG cannula. Pre-procedure anti-spasmodic oral tablet helps perform the test. It may have a therapeutic effect by flushing debris or mucus plugs from tubes.
2. Hysterosalpingo-contrast sonography – in this test uterus and adnexa are visualized ultrasonographically with the infusion of fluid through a transcervical catheter. The fluid is a contrast agent with air bubbles to aid in the identification of tubes on USG. The sensitivity for determination of tubal patency is 76-96% and specificity is 67-100%. [9]

Uterine

Uterine factors associated with infertility are synechiae, endometrial polyps, mullerian anomalies, and leiomyomas distorting the uterine cavity. The following tests are available to diagnose these factors:-

1. Transvaginal ultrasonography – allows the visualisation of most uterine pathologies. It is a cost-effective and noninvasive method for the diagnosis of intrauterine lesions with a sensitivity of 79% and specificity of 82%.
2. Saline infusion ultrasonography(SIS) – has has highest sensitivity and specificity in diagnosing uterine polyps, intrauterine adhesions, submucous myomas, and uterine anomalies.
3. Hysterosalpingography – in this, we use a contrast dye to visualize the uterine cavity.
4. Three-dimensional ultrasonography – is the most reliable investigation for examining uterine morphology.
5. MRI – it has 100% sensitivity in diagnosing uterine abnormalities.
6. Hysteroscopy - in this, we introduce a narrow telescope with a light and camera inside the uterus. It is the definitive method for diagnosing and treating intrauterine pathologies with a minimally invasive approach.

Peritoneal factors

Laparoscopy - Peritoneal factors such as endometriosis, and adnexal or pelvic adhesions may cause infertility. History and examination may raise suspicion but are not sufficient for making a diagnosis. Laparoscopy with direct visualization of the pelvic reproductive anatomy is a reliable and accurate method for diagnosing peritoneal factors. We should combine laparoscopy with hysteroscopy to make proper diagnosis and treatment of pathologies.

Male

1. Semen analysis - The semen analysis is the most important laboratory test in the evaluation of male infertility. At least two samples one week apart with 3 days of preceding abstinence should be collected by self masturbation in the laboratory or at home but the sample should be delivered within one hour of its collection.[10] If the semen analysis is abnormal repeat analysis after 3 months i.e. after completion of the next spermatogenesis cycle is advisable.

   The Lower Reference Limits of a Semen Analysis (with 95% confidence intervals) Adapted from WHO (2010)

   - Ejaculate volume: 1.5 mL (1.5–5 ml)
   - pH more than or equal to 7.2
   - Sperm concentration: 15 million/mL (12–16) (Usual normal value is >20 million/mL).
   - Total sperm count: 39 million per ejaculate (33–46 million)
   - Sperm Morphology: > 4% normal forms (Usual normal value >30%)
   - Vitality: 58% live (55%–63%).
   - Progressive motility: 32% (31%–34%)
   - Total motility: >40% (Usual normal value is >60%). If low, check for varicocele and consider an anti-sperm antibodies test.
   - Luecocyte: <1 million/ml.
   - Seminal fructose: >13 micromol/ejaculate
   - Liquefaction: 20 to 30 minutes
2. Other investigations are as per conditions or findings on semen analysis are follows:- [6]
   - Low semen volume – <1ml post-ejaculatory urine analysis to check retrograde ejaculation and transrectal USG of the scrotum to rule out ejaculatory duct obstruction and congenital absence of vas deferens and varicocele.
   - High semen volume >5ml rule out infection.
   - Oligozoospermia or azoospermia < 5 million/ml or zero sperms – hormone analysis of serum LH, FSH, and testosterone to rule out

abnormality of the hypothalamus-pituitary-testes axis. TFT, prolactin for prolactinoma, and serum cortisol at 8 pm to check for adrenal disorders.

- Karyotyping may be required to rule out Klinefelter syndrome(47XXX including variants), translocations, Y chromosomal microdeletions, or CFTR (cystic fibrosis transmembrane conductance regulator) gene mutation.
- Luecospermia - > 1 million leucocytes (pyospermia) the semen culture and sensitivity to rule out genital tract infection.
- If motility and morphology of sperms are low - USG is to rule out varicocele and anti-sperm antibodies are to be considered.
- Liquefaction time is >30 minutes then rule out infection.
- Vasography is the test to check the patency of the vas deferens and identify the precise location of vassal obstruction. It is to be done in azoospermia or severe oligozoospermia cases.
- Testicular biopsy - it is performed in suspected cases of ductal obstruction i.e. in cases of azoospermia with normal hormone levels and normal-sized testes.

CONCLUSION

The decision-making process in the infertility treatment should be primarily the cause of infertility but also the woman's age, the duration of infertility, and the previous treatment. The investigations for both males and females should be tailored based on history and examination. Blankets of investigations are not advisable for every couple.

KEY POINTS

1. Prepregancy evaluation and counseling are very important for the prevention of many conditions.
2. The initial diagnostic test for infertility should include tests for ovulation, test for tubal patency, and semen analysis.
3. Laparoscopy and hysteroscopy are not advisable in the workup of every female.
4. The purpose of evaluating males is to find out the males who can benefit from the treatment or whether ART would be beneficial.
5. In females> 40 years of age patients should be advised for ART.

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Ovulation Induction Protocol in IUI

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INTRODUCTION

The aim of ovulation induction (OI) is the induction of a single dominant follicle which is achieved by achieving a more physiological FSH threshold and window. Ovarian stimulation can improve the results of IUI by overcoming the small defects in the ovulation and luteal phase.

The indications of Ovulation induction include:

1. Anovulatory infertility
2. Unexplained infertility

Anovulation may be the cause of infertility in 25% of couples.[1] Ovulation induction is the response of the ovary to exogenous stimulation and is used in cases of anovulatory infertility.

Anovulation can be divided by FIGO into 4 types, as shown in Table 1 below: namely (HyPO-P)- [2]

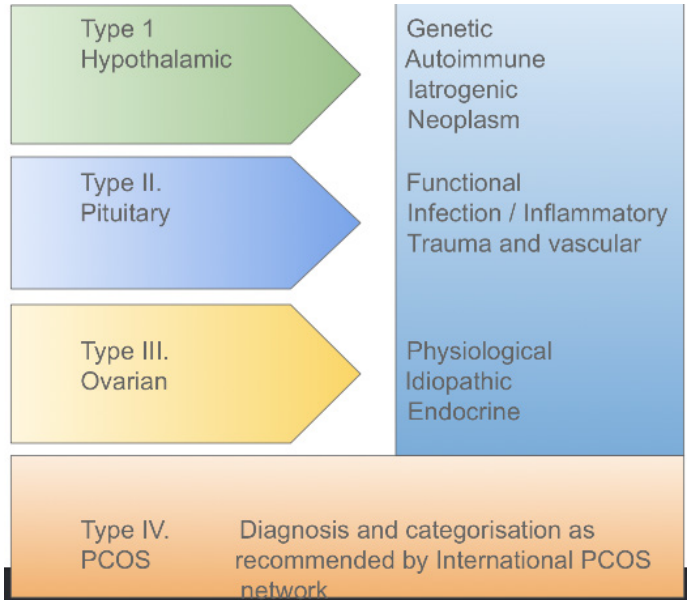

Fig. 1: FIGO classification for causes of anovulation

PHYSIOLOGY OF OVULATION

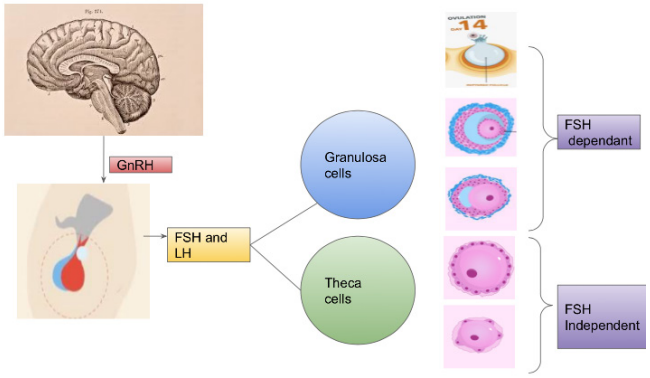

Fig. 2: HPO axis and Role of FSH and LH in Folliculogenesis

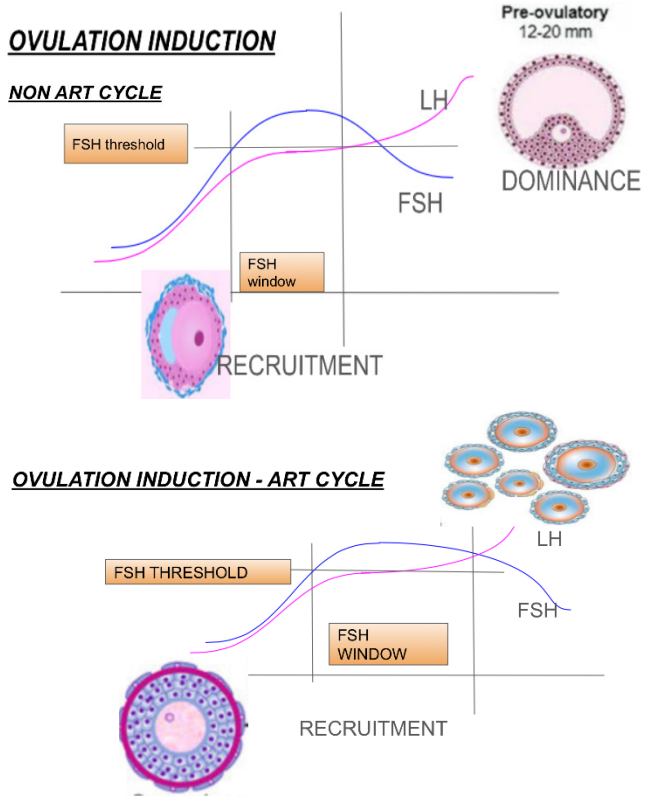

Fig. 3: Ovulation Induction in Non Art Compared to Art Cycle .

Various regimes commonly used for ovulation induction:

1. Clomiphene citrate
2. Letrozole
3. Gonadotropins
4. Clomiphene with Gonadotropins
5. Letrozole with Gonadotropins

1. Clomiphene citrate[3]

- Oral ovulogen
- Antiestrogen
- Useful in type 2 anovulation infertility
- In anovulatory infertility increases GnRH pulse amplitude
- In ovulatory women, increase GnRH pulse frequency.
- FDA approved

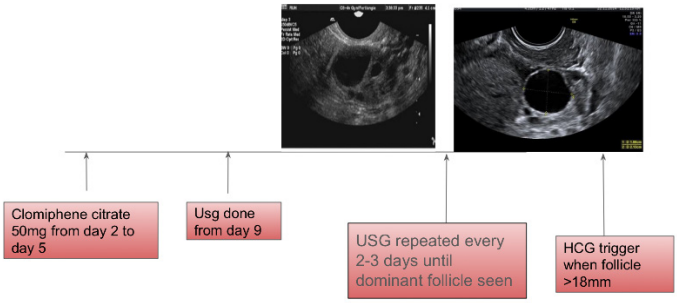

Fig. 4: Regimen if clomiphene citrate

When to stop clomiphene citrate?[3]

1. When 6 ovulatory cycles fail to yield pregnancy
2. When no ovulation with a maximum dose of 150 mg/day.

Table 1: Clomiphene citrate regimen.

Drug	Site of action	Dosage	Advantage	Disadvantage
Clomiphene citrate	Hypothalamus Pituitary Endometrium This is a selective oestrogen receptor modulator that binds to the hypothalamic oestrogen receptors. This leads to sensing a lack of oestrogen resulting in increased release of GnRH from hypothalamus and subsequently increase in FSH and LH.	Clomiphene citrate can be started from a dose of 50 mg. Started from day 2 or day 3 of the menstrual cycle. Follicle monitoring done followed by trigger when follicle size >18 mm.	Cochrane review suggests that clomiphene improves the live birth rates in unexplained as well as anovulatory infertility compared to expectant management.[4]	The antiestrogenic effect of clomiphene citrate on endometrium, cervical mucus & decrease of uterine blood flow is responsible for lower pregnancy rate. Side effects of clomiphene include - hot flushes, abdominal distension, bloating or visual disturbances.
Clomiphene Citrate - Stair Step protocol	Increment in doses of clomiphene if unresponsive to the starting dose of clomiphene.	50mg clomiphene for 5 days followed by USG on day 11-14, start with 100 mg dose immediately and do USG after 1 week, if still no response tab clomiphene started at dose 150mg and repeat USG after 1 week.	Advantage is shorter time to ovulation compared to traditional method.[5]	Not used widely as higher dose and prolonged use can have negative impact on endometrium and also increase in systemic side effects.
Clomiphene citrate with Dexamethasone or prednisolone	Act by inhibition of adrenal androgen and promoting folliculogenesis.	Dexamethasone starting from 0.5mg -2 mg or Prednisolone 5 mg OD for 5 days with clomiphene citrate 50mg -100 mg for 5 day.	Useful in clomiphene resistant women having increased DHEAS.	
Clomiphene citrate with insulin sensitisers	Insulin sensitising agents metformin and inositol help in decreasing the hepatic glucose synthesis, improve insulin sensitivity, reduce excessive steroidogenesis thus promoting ovulation, weight control and cycle regularisation.	Metformin dose of 500 mg - 1500 mg / day can be used in conjunction with Clomiphene.	Clomiphene citrate with metformin could be used instead of clomiphene citrate alone in women with PCOS to improve ovulation and clinical pregnancy rates. Metformin is preferred over inositol.[6]	Adverse effects include gastrointestinal side effects - nausea, vomiting, flatulence, diarrhoea.

Clomiphene in unexplained infertility

1. Clomiphene with IUI recommended over expectant management [7]

2. Aromatase Inhibitors

- Letrozole and Anastrozole are 3rd generation nonsteroidal aromatase inhibitors used for ovulation induction.
- Letrozole is now used as the first line for ovulation induction in anovulatory infertility.[6]
- Letrozole maintains the central feedback. As the follicle grows, increasing estradiol further suppresses FSH thus promoting mono-follicular growth.

Letrozole in unexplained infertility.[7]

1. Letrozole with IUI is recommended over expectant management in unexplained infertility.
2. No evidence that aromatase inhibitors with IUI have improved pregnancy rates as compared to clomiphene citrate with IUI in unexplained infertility.

Letrozole in Anovulatory infertility

Can be used in: -

- Clomiphene resistant cases
- Thin ET with clomiphene
- Ovarian stimulation in breast cancer cases.

Table 2 : Letrozole Regimen

Drug	Regimen	Advantage
Letrozole	1) Start from a dose of 2.5 mg / day from day 2 or day3 of the cycle after TVS suggests no cyst and ET <5 mm. 2)High doses 10-12.5mg can also be used but have risk of increased follicles.[8]	Monofollicular growth . Improved endometrial thickness and receptivity.
Extended Letrozole protocol	Letrozole 2.5mg-5 mg from day 1 to day 10 of the cycle .Useful in anovulation due to resistant PCOS.[9]	Greater number of follicles. Increased pregnancy rate.
Step Up OI protocol	Tab letrozole 2.5mg on day 2 ,2 tablet on day 3,3 tablets on day4 and 4 tablets on day 5.[10]	Higher clinical pregnancy rate but associated with multifollicular development.

Table 3: Summary of Cochrane analysis of letrozole as ovulation induction agent.

Letrozole vs clomiphene	Letroz improved live birth rates, pregnancy rates, reduced miscarriage rate and multiple pregnancy rates as per the Cochrane review 2022.[9]	Current evidence demonstrates no difference in fetal anomaly rates between letrozole, clomiphene or natural conception.[6]
Letrozole with adjuvants (INSULIN SENSITIZERS)	Cochrane analysis suggests that role of adjuncts is limited but might be beneficial in insulin resistant women.[9]	
Letrozole vs LOD	Cochrane review suggested increase in live birth rate with letrozole compared to laparoscopic ovarian drilling in women with pcos.[9]	

- Short half-life of 48 hrs, thus, fewer adverse effects on endometrium as compared to clomiphene.

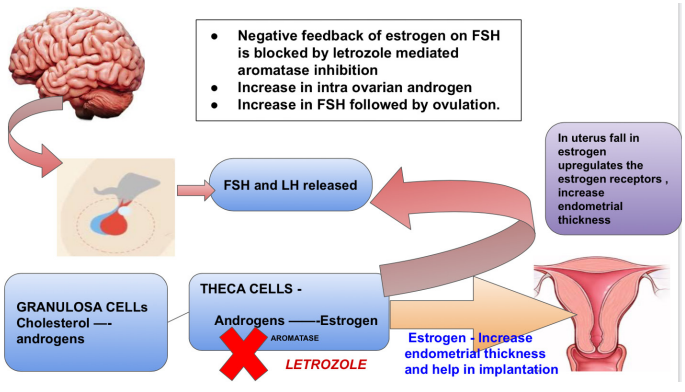

Fig. 5: Mechanism of action of Aromatase inhibitor.

3. Gonadotropins

These directly stimulate the FSH and LH release from the pituitary.

Indications:

Hypogonadotropic hypogonadism
Clomiphene / Letrozole resistance
Clomiphene / Letrozole failure

Gonadotropin Preparations

HMG
Urinary FSH / HP - FSH
Recombinant FSH

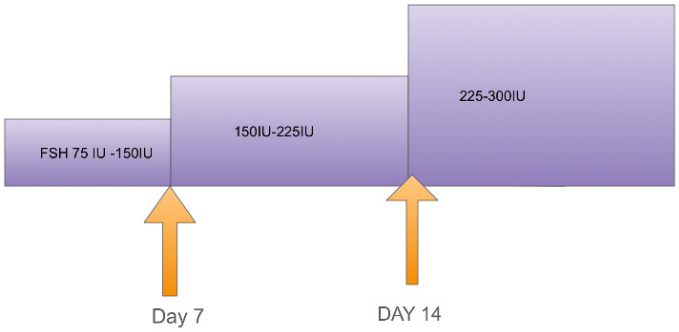

Fig. 6: Conventional step up protocol[11]

This involves administration of gonadotropin at doses above the threshold to increase the number of follicles.

Starting at a dose of 75/150 IU and increasing by 75IU every 7 days until the dominant follicle is seen and a similar dose continued till hcg trigger.

Advantage: High ovulation rates but associated with high complications of multiple pregnancies.

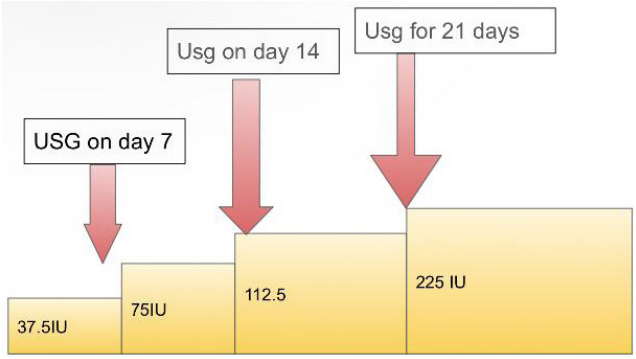

Fig. 7: Low dose step up protocol[11]

- Preferred method of ovulation induction in PCOS.
- Starting from a dose of 37.5/75 IU daily for 7 days.
- Small dose increments done at weekly intervals.
- USG done on day 7 if follicle <10mm increase the dose by 37.5 IU and if follicle >10 mm continue with the same dose till hCG triggers.

Advantage

- Useful in resistant PCOS
- Complications like multiple pregnancy and OHSS are less with this regimen.

Disadvantage:

- Multiple injections required
- Prolonged regimen

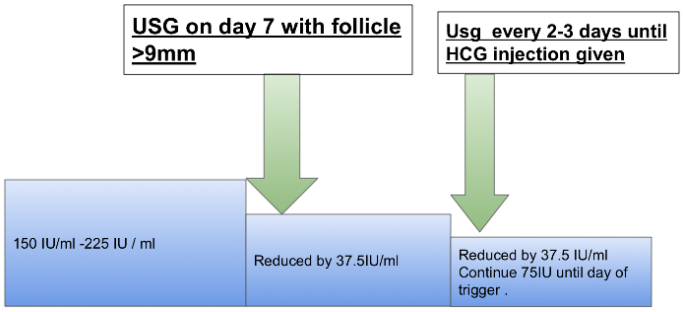

Fig. 8: Step down protocol[12]

1. Principle - Early follicular rise of FSH with subsequent decline after dominant follicle is selected.
2. Start from a higher dose of 150-225 IU / day followed by USG on day 7. If no follicle >9mm then increase the dose by 37.5 IU. If follicle >9mm continue with the same dose until HCG trigger.

Disadvantage:

1. An experienced physician needed to determine the effective dose of FSH/ HMG
2. Stringent monitoring needed.

Table 4: Gonadotropin with CC/Letrozole

Drug	Regimen	Advantage	Disadvantage
Gonadotropin with CC	In this regimen 100mg CC given from day 2- day 5 and inj FSH / Hp HMG 75 is given on day 6-8. Alternatively Tab CC 100 mg from day 3 for 5 days and Inj HP HMG 75 IU from day 6 until HCG trigger.13	1)Cost effective 2)Useful in CC resistant cases. 3)Higher pregnancy rate. 4)Lower rate of multiple pregnancy and OHSS than gonadotropins alone.	Antiestrogenic effect of clomiphene can have a negative impact on pregnancy rate . Increased monitoring. Multiple hospital visits.
Gonadotropin with Letrozole	Tab Letrozole 2.5 mg from day 3 for 5 days with Inj HP HMG 75 IU from day 6 until HCG trigger.13	Endometrial thickness and pregnancy in Letrozole with HMG is higher compared to CC with HMG (14) Lower rate of OHSS and multiple pregnancy compared to CC with gonadotropins. Reduced dose of gonadotropin needed.	Increased monitoring needed and more hospital visits.

Gonadotropin could be the second-line pharmacological therapy for PCOS who have failed first-line ovulation induction.

No difference in pregnancy rate was found between FSH and HMG.[14]

Gonadotropin alone can be used instead in combination with clomiphene for anovulation infertility.[6]

Gonadotropins in Unexplained infertility[7] – Low-dose gonadotropin is not recommended over oral agents in unexplained infertility due to cost concerns and increased rates of multiple pregnancies.

When gonadotropin treatment is considered, the following should be taken into account:

Table 5: Summary of Drugs used in ovulation Induction

Drug	Route of administration	Outcomes
Clomiphene citrate	Oral agent	Ovulation rate : 70-80% Pregnancy rate : 15-22% Failure (no pregnancy despite ovulation) -40% Resistance -25% Multiple pregnancy rate : 8-10%16
Letrozole	Oral agent	a)Ovulation - 75% b)Pregnancy -40% c)Multiple pregnancy rate - 5% 9
Gonadotropin	Injectable	Ovulation rate - 70% Pregnancy rate with gonadotropins - 20% per cycle17 Multiple pregnancy - 36% 18

- The cost of ovulation induction may rise
- Expertise required
- Intensive USG monitoring
- Prefer low-dose-step up protocol to optimize the chance of mono follicular development.
- Luteal support following gonadotropin for ovulation induction is beneficial[15]

CONCLUSION

Ovulation induction (OI) and intrauterine insemination are often recommended as first-line treatment in some cases of male infertility, advanced age, and endometriosis. It is essential to know which factors are important in determining the outcome of COH-IUI and accordingly, the appropriate inducing agent is used before IUI.

KEY POINTS

1. Ovulation induction aims at mono follicular development.
2. Letrozole is the first-line ovulation induction agent.
3. Clomiphene citrate's anti-estrogenic effect can compromise efficacy.
4. Letrozole can be used in clomiphene-resistant cases.
5. Adjuvants used along with clomiphene or letrozole can be beneficial.
6. Gonadotropins are used as second-line ovulation induction agents in anovulatory infertility but are associated with increased multiple pregnancy rates.
7. In Unexplained infertility ovulation induction with IUI is recommended over expectant management.

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Monthly Clinical Meetings AOGD Calendar 2024-25

Date	Hospital
26th April, 2024	LHMC & Smt. Sucheta Kriplani Hospital
31st May, 2024	B L Kapoor Hospital
28th June, 2024	Apollo Hospital
26th July, 2024	Army Hospital (Research & Referral)
30th August, 2024	AIIMS Delhi
27th September, 2024	ESI, Basaidarapur Delhi
25th October, 2024	DDU Hospital
29th November, 2024	MAMC & LNJP Hospital
27th December, 2024	Sir Gangaram Hospital
31st January, 2025	VMMC & Safdarjung Hospital
28th February, 2025	UCMS & GTB Hospital
28th March, 2025	RML Hospital
25th April, 2025	LHMC & Smt Sucheta Kriplani Hospital

Assisted Reproductive Technology in Infertility

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Infertility is on the rise with changes in lifestyle, delayed childbearing, and environmental factors. Males were earlier only responsible for 25% of fertility problems but now it is seen that over 40% of men have suboptimal sperm counts.[1] Low ovarian reserve, endometriosis, and PCOS are also found at an increased incidence. The treatment in these cases is Assisted Reproductive Techniques (ART) like Intrauterine insemination (IUI) and Invitro Fertilization (IVF). IUI is a basic intervention in a sub-fertile couple where tubes are patent and semen parameters are not extremely low. In IVF with advanced techniques, the oocyte is retrieved and then fertilized outside the body (in vitro) to form an embryo which is transferred into the uterus.

INTRAUTERINE INSEMINATION

IUI is the direct placement of processed, motile sperm, washed free of seminal plasma and other debris into the uterus as close to the ovulated oocytes as possible. It reduces the distance of travel and increases the available spermatozoa at the site of fertilization.

Indications

1. *Female factor*
   - Anatomic defects of the vagina or cervix
   - Sexual dysfunction
   - Mild to moderate endometriosis
   - Endocrine anomalies
   - Ovulatory dysfunction
2. *Male factor*
   - Mild Male subfertility: e.g. Mild oligozoospermia, asthenozoospermia, or teratozoospermia
   - Anatomic defect of penis e.g. Hypospadias
   - Sexual/ejaculatory dysfunction
   - Retrograde ejaculation
   - Semen volume in excess or deficit
   - Immunological factors
3. *Other factors*
   - Unexplained infertility
   - Combined subfertility factors.

Procedure

IUI is the primary ART procedure used in infertility to overcome a wrong timing or difficulty in intercourse, aberrant ovulation, or a semen factor. The female partner is given oral or injectable ovulogens and follicular monitoring is done to identify when the dominant follicle reaches 18-20 mm. An endometrial thickness of 8 mm or more is to be ensured. The ovulation trigger i.e. injectable hCG is given and IUI is timed with the follicular rupture 36-38 hours later. The semen is collected on the day of IUI and processed to isolate motile sperms and remove seminal plasma. Semen processing is done by swim up or density gradient method which involves centrifugation and washing to remove seminal plasma and debris. This is concentrated in 0.5 ml media and deposited into the uterine cavity with an IUI catheter.

Success rates

It has a success rate of about 15% in unexplained infertility and mild male factors. Per cycle pregnancy rate of 10.9% and a cumulative pregnancy rate of 19.4% was found in a study.[2] The probability of pregnancy was negatively associated with females aged ≥ 35 years, endometriosis, unilateral tubal factor, or anatomical alteration, and total progressive motile sperm count (TPMSC) < 5.

INVITRO FERTILIZATION

IVF involves the retrieval of oocytes from mature follicles by an oocyte retrieval needle transvaginally under ultrasound guidance. The oocytes are incubated with the sperm for fertilization and the embryo formed is transferred to the uterus at an appropriate time.

Indications of IVF

1. Indication in the male partner
    - ***Poor sperm count and motility***: In men with oligoasthenozoospermia- intracytoplasmic sperm injection (ICSI) is performed and the sperm is directly injected into the oocyte by a microneedle under the microscope.
    - ***Azoospermia*:** In men with absent sperms in ejaculate, surgical sperm retrieval is done through Testicular aspiration or Microtese (opening the testis under the microscope to identify dilated tubules that may contain sperms).
    - ***Retrograde ejaculation*:** In these cases, sperms are collected from the urine and ICSI is done.
2. Indications in female partner
    - ***Blocked Fallopian tubes***: in case of severe endometriosis or pelvic inflammatory disease.
    - ***Endometriosis:*** Grade IV endometriosis with pelvic adhesions and large endometriotic cysts
    - ***Failure of IUI treatment***: Women repeatedly do not respond to intrauterine insemination (IUI) procedures
    - ***Donor oocyte:*** As women get older, their ovarian reserve gets exhausted and they will need a donor oocyte. Younger women may require a donor oocyte in cases of premature ovarian insufficiency, decreased ovarian reserve after chemotherapy or ovarian surgery, and in genetic conditions like fragile X syndrome and Turner Syndrome (mosaic).[3]
    - ***Surrogacy:*** Surrogacy would be needed for women with an absent uterus (by birth or after surgical removal) or with a uterus damaged with dense intrauterine adhesions not amenable to surgical treatment. Cases, where pregnancy is to be avoided because of medical conditions like severe pulmonary/kidney/heart disease or uncontrolled diabetes, would also need surrogacy.
3. Indications in both/either partners
    - ***Fertility preservation:*** Fertility preservation is a term used where gametes or embryos are cryopreserved in liquid nitrogen. It can be used for cancer patients (Oncofertility) before they undergo chemotherapy and radiotherapy. These gametes and embryos can be stored for 10 years. Recently, ovarian tissue freezing has also been recognized as an acceptable method of fertility preservation- used in young women and preadolescent girls undergoing cancer treatment to preserve fertility.[4] Both natural and IVF pregnancies can occur after this procedure. It has the advantage of being done immediately unlike in oocyte freezing where 9-10 days of stimulation is required and chemotherapy may have to be delayed. Fertility preservation is also being used in women with endometriomas before surgery as ovarian reserve is known to decrease after removal of endometrioma.
    - ***PGT – Preimplantation genetic testing:*** a few cells in the embryo are biopsied and sent to test for genetic normalcy. Either or both partners may have a genetic disease that they want to avoid in their child. Testing is indicated in older women, recurrent IVF failures, and miscarriages to rule out a genetic cause.[5]
    - ***Viral Infections***: In couples where one or both of the partners are HIV or Hepatitis B or C positive, natural conception puts the partner and child at risk for infection.[6,7] Sperm washing and injecting into the oocyte minimizes transmission to the woman and the child.

Procedures

Gonadotropin injections are given to stimulate the ovaries so that all the basal follicles grow to yield mature oocytes capable of fertilization with sperm to yield embryos which are transferred with a catheter into the uterine cavity.

Controlled Ovarian Stimulation

It is important to identify factors predicting the response of the patient. This can be done by taking into account the response to the previous cycle, weight/BMI, age, ovarian reserve markers like AMH, antral follicle count day 2 hormones, and other factors that determine whether the patient is poor or hyper responder like the cause of infertility (PCOS, endometriosis, etc), or previous ovarian surgery.

1. **Age:** Prescribing higher doses in older patients is often done because a woman's ability to respond to ovarian stimulation declines with advancing age
2. **BMI:** Women with higher BMI require increased doses of gonadotropins.[8]
3. **Ovarian reserve markers:** The ovarian reserve markers used most in clinical practice are AMH and antral follicle count (AFC). Although these markers tell us about ovarian response they do not predict pregnancy.
4. **Previous Response:** If the number of oocytes retrieved in the previous cycle is adequate as per AFC, then it is best to start with the same doses.

The response to stimulation is monitored with serial measurements of serum oestradiol and transvaginal ultrasound imaging of ovarian follicles. In general, the goal is to have at least 3 follicles measuring 17-18 mm in mean diameter, ideally accompanied by a few others in the 14-16 mm range and a serum oestradiol concentration that is consistent with the overall size and maturity of the cohort (approximately 200 pg/mL per follicle measuring 14 mm or greater). Injectable HCG or a GnRH agonist is given as the final trigger for maturation.

1. ***Oocyte Retrieval***: Oocyte pick-up is planned for 34-36 hours after hCG is given. The aspiration is done transvaginally under ultrasound guidance with a needle attached to a suction pump which with negative pressure aspirates the follicular fluid along with oocytes into a test tube.
2. ***Laboratory procedure- Insemination***: Fertilization takes place in droplets of semen prepared in a dish. Alternatively, if there is a poor motile count of semen then an ICSI is performed where a micropipette holds and positions the oocyte while the sperm is injected through a microneedle under an inverted microscope. It is cultured in the incubator at 37 degrees C for 3-5 days. Fertilization check is done after 16-20 hours. The embryos are graded as per their quality on day 3 and day 5 to segregate the best quality ones for transfer into the uterus.
3. ***Embryo transfer:*** Assessment of uterus and endometrium are important -Endometrium should be at least 8 mm thick with a good blood flow and morphology- assessed by Doppler ultrasound. There are 4 zones identified in the endometrium and blood flow should be present in the innermost zones. If the endometrium is suboptimal, embryo transfer should be deferred to the next cycle. A blastocyst or day 5 culture has a higher chance of implantation and pregnancy. It is done on a partially full bladder under ultrasound guidance A soft catheter for embryo transfer is used as it causes minimum trauma when inserted, thus not disturbing the endometrium or inducing uterine contractions which may expel the embryo. Usually, two blastocysts are transferred. The rate of successful implantation is lower in older women or those with recurrent IVF failures and thin endometrium.[9] Embryos that are not transferred may be stored by cryopreservation in liquid nitrogen.

Adverse effects of IVF

Stimulation of ovaries with gonadotropins can cause enlarged ovaries, nausea, and bloating. There can be multiple pregnancies if more than one embryo is transferred. Ectopic pregnancy may occur. Serious complications of egg retrieval are uncommon, but side effects such as pelvic cramping, light bleeding, and vaginal discharge often occur. Ovarian hyperstimulation syndrome (OHSS) may occur when ovaries are overstimulated leading to ovarian enlargement and abdominal swelling. This can cause severe abdominal pain, vomiting, and if untreated, blood clots in the legs or lungs and fluid imbalances in the blood. In recent years, most clinics have gone on to OHSS-free clinics by utilizing a GnRH agonist instead of hCG as an ovulation trigger, avoiding fresh embryo transfer or canceling IVF cycles in overstimulated ovaries. In preventing hyperresponse, it is also important to identify a hyperresponder to ensure they get a lower dose of FSH.[10]

Special Procedures

Assisted reproductive technologies have progressed over the last 40 years to give optimum success rates and options.

1. ***Laser-Assisted Hatching***: The outer covering of the embryo, known as the zona pellucida may sometimes be too thick or hard. Laser hatching is indicated in older women, frozen embryos, or those with recurrent implantation failure.
2. ***Rejunevative therapies for thin endometrium***: Intrauterine instillation of platelet-rich plasma (PRP), Granulocyte colony-stimulating factor (GCSF) and stem cells [11]
3. ***Testing Microbiota of Uterus***: Recurrent implantation failure or miscarriages are now thought to be due to altered microflora of the uterus as is seen in the gut. In case of altered flora, a vaginal probiotic is prescribed.
4. ***Preimplantation genetic testing (PGT)*** — In PGT after drilling a hole in the zona of the blastocyst (Day 5 embryo) with the laser, a few cells are removed and sent for genetic analysis. Patients can have their embryos tested before transfer and discard embryos that have a genetic mutation, hence transferring only those that are normal.
5. ***Dual Stimulation and Embryo Pooling for Low Egg Reserve***: Women who have an extremely poor egg reserve may undergo a dual stimulation where two oocyte retrieval procedures are done in the same cycle – one in the follicular phase and the other in the luteal phase. Pooling the oocytes or embryos formed increases their number for transfer thus improving chances of pregnancy and decreasing dropout rates after a suboptimal cycle.[12]
6. ***Autologous Stem Cell Ovarian Transplant (ASCOT) and Platelet-rich plasma (PRP):*** Stem cell transplant and PRP are injected in the ovarian cortex with the oocyte retrieval needle in women with depleting follicular pool due to low ovarian reserve. This can be done transvaginally under ultrasound guidance or laparoscopically. This procedure is experimental and is done to regenerate the follicle pool.[13]
7. ***Ovarian Tissue cryopreservation:*** now recognized as a regular technique with removal of experimental label.
8. ***Microtese for Azoospermia:*** In case of absent sperms in ejaculate (azoospermia) testicular sperm may be retrieved surgically.If absence is because of obstruction, a simple needle aspiration is needed. In nonobstructive azoospermia where the production of sperm is impacted an advanced treatment to retrieve testicular sperm is Microtese. The advantage is that very minimal testicular tissue is removed unlike in open biopsy where the pieces removed are larger.

Success rates

IVF has a reasonable rate of success in most cases. Overall, 50 to 55% of patients have a positive beta hCG on testing. Approximately, 35 % of IVF cycles will end in a live birth. However, an individual's chance of success depends on several factors, including age, cause of infertility, and treatment approach.

CONCLUSION

Infertility is on the rise with changes in lifestyle, delayed childbearing, and environmental factors. Low ovarian reserve, endometriosis, PCOS, and male factor infertility are such conditions where ART is useful.

KEY POINTS

1. IUI has a success rate of about 15% in unexplained infertility and mild male factors.
2. Ovarian tissue freezing is the only technique available to preserve fertility in preadolescent girls where oocytes cannot be retrieved.
3. A blastocyst or day 5 culture has a higher chance of implantation and pregnancy than a day 3 embryo.
4. The advantage of MicroTESE is that very minimal testicular tissue is removed unlike in open biopsy where the pieces removed are larger.
5. Stem cell transplant and PRP are injected in the ovarian cortex with the oocyte retrieval needle in women with depleting follicular pools due to low ovarian reserve.

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How to Set Up an IVF/ART Center

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Infertility affects 7-10% of the Indian population.[1] The patient ordinarily moves from a general physician or a gynecologist to an infertility specialist. Once an indication for ART/IVF (Assisted reproductive technology/In vitro fertilization) is realized, the hunt for a good IVF Centre begins. IVF Lab/center is a tertiary-level infertility clinic or a level two ART clinic. It is not only the knowledge, skill, and experience of the clinician, embryologist, and lab personnel but also the teamwork and quality control at the ART Centre that define the results of the IVF procedure.

Setting up an IVF center starts from the creator's mind. A small Infertility center with minimal equipment may be sufficient for one's private practice. However, a center attached to a medical college needs to address the need for expansion with an increasing load of patients and also the need for research and clinical training. Hence, the center's infrastructure, equipment needed, manpower requirements, etc., will vary. The cost of the project and recurrent costs need to be considered. Nevertheless, all ART centers in India must follow the guidelines provided by ART and Surrogacy Act 2021. An international expert meeting (Cairo Consensus) established 50 points regarding site suitability and design criteria for new construction and laboratory commissioning.[2]

Prerequisites for Space Allocation for an ART Center

- An ART center should avoid being close to petrol pumps, chemical and cement storehouses, heavy traffic, and parking slots.
- The second floor is ideal as there is less disturbance and the basement should be avoided, any damp area or water seepage should be checked for. Connectivity with lifts/elevators should be there as transportation of gas cylinders, LN2, etc., will be needed.
- The center should be far from radiation sources in the hospital, i.e. CT scans, radiotherapy units, or waste disposal areas. These in turn should be away from the exhaust emission areas and backup power generators. The total area depends on the expected workload.
- Vermin proofing is planned and implemented before the IVF unit becomes functional, as pesticide use cannot be done once the unit is functional.

INFRASTRUCTURE OF IVF CENTRE

It should be a coordinated effort of engineers, architects, clinicians, embryologists, and technical staff who are going to work there. Consideration should be given to the most recent updates in facilities, equipment, and procedures. The walls of an IVF center should be smooth with no cracks and crevices, easy to clean, non-porous, and non-odorous thus minimizing Volatile Organic Compounds (VOC) release and embryotoxicity. Epoxy paints emit VOCs (amine) and take several weeks to cure. Epoxy paint should be used only after ensuring the burn-in period. Emission testing on samples is required since amine catalysts can be very persistent. Paints containing formaldehyde, acetaldehyde, isocyanates, reactive amines, or phenols should not be used as they have soluble VOCs.

Walls & partitions should be of nonporous material such as panels made from aluminum tri-hydrate – these are inert (low VOC), hypo-allergenic, easy-to-clean, and inexpensive. The ceiling must be made of a contiguous, solid material. Essential access panels must have air-tight silicone gaskets as a sealant. False ceilings should be avoided. Ecologically suitable, water-based paints with acrylic, vinyl, or acrylic latex polymers should be used. The flooring should be slip-resistant, non-staining, and non-permeable.

Steel and not wooden furniture should be used. These furniture items should be cleaned thoroughly with isopropyl alcohol to remove any superficial VOCs before introduction into the laboratory. The grease used to lubricate hinges and drawer slides should be silicone-based. Doors must be tight-fitting with bottom '''sweeps''' and perimeter seals (top and edges); coated or made of steel; and pass-through windows are preferred. Provisions should be made so that doors are wide enough to accommodate large equipment (e.g., incubators) after the lab becomes permanently sealed and operational. Sterile areas, especially OT and labs, should have positive pressure to facilitate airflow from inside to outside.

Attention should be given to operator comfort to provide a safe working environment that minimizes the risk of distraction, fatigue, and subsequent mistakes.[3] Considerations should include bench height, adjustable chairs, adequate work space per person, microscope eye height, efficient use of space and surfaces, sufficient environmental lighting, and air-conditioning with controlled humidity and temperature.

Mimicking an in vivo atmosphere is extremely important to optimize fertilization, cleavage, blastulation, implantation, and pregnancy rates. Embryos and culture media are mostly in incubators with controlled temperature and CO2 conc, pH, and humidity. But gametes/embryos are taken out for performing ICSI, assessing fertilization & growth, changing media, and other procedures like LAH or Embryo biopsy for PGD/S.

LIGHTING AND POWER IN IVF CENTER

Sealed lighting units are preferred to help reduce airborne particles and these should be dimmable. Yellow white color light is less damaging than cool white light. Direct Sunlight, UV light, & Fluorescent light are detrimental to embryos (incandescent light is better) at 200 lux lighting. Power sockets should be plenty, at a regular distance and more than estimated.

The total load should be calculated after adding up each piece of equipment, and backup UPS/INVERTER/different electrical phases should be in place. Critical areas, i.e., IVF Lab, Media storage refrigerators, and incubators for embryos and gametes, should have zero tolerance to power breakdown.

HVAC (Heating, Ventilation, and Air Conditioning System)

HVAC delivers clean air to the room, removes contaminants, and pressurizes the room. Controls temperature and humidity and thus creates an optimal environment for embryo culture and viability. The system includes activated carbon and/or KMnO4(potassium permanganate) to remove VOCs. High-efficiency particulate air (HEPA) filters are used to remove particle sizes of 0.3 microns and, thus, 99.97% of airborne particles. UV light (optional) can be used for eliminating microbes & photooxidation of VOCs. Positive pressure, which is the ideal target, is +38 to +50 Pa in the IVF laboratory (recommended minimum +30 Pa). To minimize air contamination, the Embryology lab should be positive to the OT, which is positive to the ET room/hallways.

Air changes should be 15 total air changes per hour, including three fresh air changes per hour, i.e.20% outside air. Any construction activity in the surroundings has a very negative effect on the results and thus should be monitored. Temperature in the lab should be typically within the range of 20–24°C. Incubators should be kept at 37^{0}C and 6% CO_2. Relative room humidity should be between 40% and 45%. Higher levels will promote the growth of molds; lower values cause high levels of evaporation during dish preparation, which will affect the osmolarity of the culture medium and is deleterious to embryos in culture.

- Ideal VOC <0.2 ppm, preferably 0
- VOC > 1ppm – directly toxic to embryos
- VOC meter- can measure till 0 ppb
- Aldehydes are very toxic for embryos; they should be 6<5 micrograms/m3.

The entire area is divided into two parts- a non-sterile and a strictly sterile area. The sterile area has OTs, an embryo transfer room, and an embryology lab complex. The rest is the nonsterile area which includes a reception and waiting room for patients, a room with privacy for counseling and interviewing. It also includes washrooms for lab personnel and other staff of the IVF center, a semen collection room with an attached toilet, consultant's room to examine male and female partners independently. A room for an ultrasound machine to perform ultrasound of pelvic organs and estimate AFC, as well as do follicular counting. A general-purpose clinical laboratory, a storeroom for keeping essential stock of both sterile items and nonsterile items in the facility to keep refrigerated items as needed. A record room with a computer is used to save the details of patients' records, results, and treatment given, as well as any adverse event, outcome, and follow-up advice.

Semen Collection Room

This room should be private, located in a secluded area close to the laboratory, and soundproofed. It should have a washbasin, soap and clean towels, and a toilet at the end of the hallway, and it must not be used for any other purpose. There should be a provision for the safe delivery of samples to the andrology lab and for disabled persons to have access. It should fulfill the requirements for couples, with a facility for audio-visual stimulation.

Semen processing laboratory/Andrology lab

In this lab, semen is sampled for diagnostic purposes, and sperm processing is done for ART. It should be close to the semen collection room. This equipment is sufficient for centers performing only IUI.

- Laminar air flow
- Centrifuge machine
- Facilities for microscopic examination
- Refrigerator
- Heating block
- Sperm Counting Chambers such as Makler Chamber / Neubauer Chamber.

A separate room with an appropriate table for performing IUI should be there.

STERILE AREA

The sterile area must be air-conditioned, and fresh air filtered through an approved and appropriate filter system circulated at ambient temperature (22-25^{0}C). IVF procedure lab/OT, in which procedures such as oocyte retrievals, embryo transfers, and percutaneous sperm retrievals are carried out, should be differentiated from invasive surgical facilities. Consequently, if the ART procedure room is to be used for invasive surgical procedures, its HVAC system should be separate from the ART suite.

OPERATION THEATRE

This is for performing Ovum pick up under ultrasound guidance. It should have an anesthesia workstation and emergency resuscitative drugs. There should be a provision for transferring the patient for laparotomy/laparoscopy immediately if there is any complication. Another OT for intrauterine transfer of embryos is a bonus, though the same OT can be used. OT should have a pass window for COC transfer to the embryology lab. The embryology lab should have a separate entrance to the lab and not through OT, preferably. OT should have an anteroom or an area for changing footwear and changing into a sterile gown after surgical scrub. Entry to OT and Lab should be strictly controlled.

Sperm Preparation and Cryopreservation Area

Liquid nitrogen containers and medical gas cylinders are preferentially placed immediately adjacent to the laboratory in a closet or small, ventilated room with outside access. Pipes and tubes enter the laboratory from this room, and cylinders can be delivered to this room so that the laboratory area is not compromised in any way. Medical gases can be directed into the laboratory using pre-washed vinyl/Teflon-lined tubing such as fluorinated ethylene propylene, which has high humidity, temperature, and UV radiation stability[4]. Lines should be properly marked on every meter indicating the incubators supplied to facilitate later maintenance. The soldered or brazed copper lines should be avoided wherever possible as they cause continuous contamination; copper lining if used should be cleaned and purged for a prolonged period before use in the laboratory. Microbial sampling for aerobic bacteria and fungi should be periodically done.

The IVF laboratory must have a cleaning facility for surgical instruments. Autoclaves should be placed in a tight-built room with released steam exhausted directly outside of the building and not on the IVF laboratory's HVAC system. This keeps the relative humidity in the facility to controllable limits. Ample storage space should be there outside the IVF lab as inside storage produces VOC. Each workstation and microscope should have a still camera and/or video camera and monitor.

The duties of an embryologist are to safely perform gamete and embryo handling along with culture procedures and to be a professional witness to another embryologist in the lab. Ideally, an embryologist should be able to finish one complete procedure without moving more than 3m meters in any direction. KPIs like live births per embryo and cumulative data from fresh and cryopreserved cycles are considered objective assessments.

Personnel/Manpower

Gynaecologist, Ultrasonologist (ideally, a gynecologist should do TVS ultrasound & follicular monitoring), Embryologist, Counselor, Nurses, Andrologist, Housekeeping staff, OT technician, and Anesthetist. Their number will vary with the load in the clinic. Once the lab is set up, Validation of the lab may be done by an external agency using various parameters.

Equipment Needed in IVF Lab

General gynecology instruments with trays should be available. Special equipment includes a micromanipulator with an inverted microscope for ICSI, stereo zoom microscope for OCC (oocyte cumulus complex)hunting and embryo assessment, trinocular microscope/binocular phase contrast microscope for semen examination, oocyte aspiration pump, ultrasound machine with TVS probe, Tri gas/CO2 Box incubators/benchtop incubators, witness system, laminar air flow hood, culture media, disposables/consumables, cryo tanks and equipment for cryo freezing, Centrifuge machine should be available for semen processing, temperature meter, VOC meter and Ph meters. The tender agreement for all equipment must have an AMC/CMC for five years. Also, twice the number of this equipment should be there except the micromanipulator, as there can be a breakdown needing urgent backup. Incubators used should be separate for semen preparation and embryo culture, as well as media/dish preparation. Embryoscope and laser may be added as the need arises for ICSI in cryopreserved oocytes and for Prenatal blastomere biopsy.

Burning in of the Finished Facility

A typical burn-in consists of increasing the ventilation rate and increasing the temperature of the new area by 10°C–20°C; even higher temperatures are acceptable[5]. This combination results in the removal of the volatile organics. The air handling system should be properly configured for the burn-in of the newly constructed area once construction is finished. As previously stated, the system must be capable of supplying the space with air at a temperature of 30°C–35°C and relative humidity at less than 40%. The IVF laboratory should be kept closed during the burn-in period which can range from 10 to 28 days.

Future Innovations in the Horizon

Future research and innovation are fast catching up with the use of robotics for micromanipulation, cryopreservation, and cryostorage. A lot of automation in labs is anticipated by 2030[6]. Among them is Iris recognition at microscopes and workstations, which automatically records the date, time, process, and scientists in the electronic medical records system. How much of it will be reproducible in our labs, and when? Needs to be seen. The coming up of laboratory on a chip maybe!!

CONCLUSION

Apart from the knowledge, skill, and experience of the clinician, embryologist, and lab personnel, it is the teamwork and quality control at the ART Centre that define the results of any IVF procedure. All ART centers in India must follow the guidelines provided by ART and Surrogacy Act 2021.

KEY POINTS

1. The ambient atmosphere in the lab must be maintained and controlled in terms of temperature, humidity, and air quality.
2. IVF center is a coordinated effort of engineers, architects, clinicians, embryologists, and technical staff who are going to work there
3. Timely audits must be done to ensure quality control in the lab

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Ovarian Rejuvenation - PRP and Stem Cell Therapy

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INTRODUCTION

Background

The spectrum of patients coming for Infertility treatment has undergone a paradigm of change. With the rising number of women opting to pursue professional careers, the age of marriage has been pushed from the early 30's to the late 30's. This has led to more women wanting their biological child in the late 30's to early 40's. The ovarian reserve sharply declines by 35 years hence the need to look at options to get back ovarian function. Ovarian aging is associated with age-related decline in oocyte quality & quantity. Also along with age-related decline in fertility, there is another class of patients who at a young age have a diminished Ovarian reserve. This includes premature ovarian insufficiency (POI), poor ovarian response (POR), and diminished ovarian reserve (DOR) for controlled ovarian hyperstimulation (COH). Patients belonging to these categories too are patients who require ovarian rejuvenation. Premature Ovarian Insufficiency is characterized by raised Gonadotrophin levels, low estradiol levels, and menstrual abnormalities(oligomenorrhoea, amenorrhoea)in women less than 40 years of age. As per the consensus by ASRM in 2020, Decreased Ovarian Reserve is defined as a decline in oocyte quality, oocyte number, and reproductive potential. Poor responders are categorized according to Poseidon's criteria which help in categorizing poor response patients and the preferred protocol to be used for ovarian stimulation.

Utility: Almost 5-35% of IVF cycles are associated with a sub-optimal response. Different additional measures have been applied to increase the response which could be increasing Gonadotropin dose, luteal stimulation, using aromatase inhibitors and adjuvants. Despite using the above measures ovarian function doesn't get restored, hence Ovarian rejuvenation has become very relevant in this scenario of declining ovarian reserve. Different modalities have been tried to rejuvenate the ovaries the most promising being: Ovarian PRP (Platelet Rich Plasma) Injection and Stem Cell Injection. Autologous PRP initiates the development of isolated human primordial and primary follicles to the preantral stage. Ovarian PRP involves extracting a patient's blood, processed to concentrate the platelets, and creating PRP. The PRP is then injected into the ovaries to stimulate rejuvenation.

Stem cells for ovarian rejuvenation: Stem cells derived from different sources have been used for rejuvenation in the reproductive system. Stem cell injection prevents granulosa cell apoptosis which as a result improves ovarian function. Injection in the ovary leads to restoration of ovarian function and avoids the use of donor oocytes.

Routes of administration: Both PRP and Stem Cells can be injected either under transvaginal Ultrasound Guidance or by laparoscopic guidance when ovaries are poorly visualized. These are injected in both ovaries with a 35 cm 17 G single-lumen needle.

Need of Review: These methods of Ovarian rejuvenation need to be reviewed to analyze their potential benefits to restore ovarian function vs side effects and if at all they lead to an increase in pregnancy rate.

Discussion

Ovarian rejuvenation with Platelet-Rich Plasma(PRP)

In Women with DOR and POI, there is a disruption of the molecular mechanisms mediating neoangiogenesis. Autologous PRP, rich in PDGF, VEGF, and TGF-β, activates the neo-angiogenesis process, thus improving ovarian function. PRP is also rich in other growth factors like HGF, IGF, and EGF which also improves follicle maturation and ovulation. Studies have shown that PRP has the potential to restore the hormone balance between AMH, FSH, E2, and LH and thus increase pregnancy rates and live birth rates.[1] The neoangiogenesis after Ovarian rejuvenation with PRP essentially supports the growth of the secondary pre-antral follicles to large ovulatory antral follicles.[2] The HPA Axis is positively affected by intracellular signaling pathways like proliferation, migration, and protein secretion after PRP instillation.[3] The PRP also has immunomodulatory and anti-inflammatory properties due to the presence of Hepatocyte Growth Factor (HGF), indoleamine 2,3 dioxygenase, galectins, and others.[4] The factors like neurotrophins, granulocyte colony-stimulating factor

(G-CSF), granulocyte-macrophage colony-stimulating factor (GM-CSF), stem cell factor (SCF), connective tissue growth factor (CTGF) and growth hormone (GH) act synergistically to induce the effects of PRP.

Neo angiogenesis after PRP instillation improves intrafollicular oxygen and helps in the recovery of mitochondrial function and improvement in follicular growth and oocyte quality followed by high fertilization rates and ongoing pregnancy rates.[5,6]

Preparation of PRP-13.5ml blood to be collected in two 15ml tubes with 1.5 ml of anticoagulant (Acid citrate dextrose solution) each. A ratio of 1ml anticoagulant to 9ml blood should be maintained. Centrifuge for 15 minutes at 2000 RPM (soft spin). Plasma rich in platelets is separated with at least 50% of volume with no buffy coat on the RBC layer. Transfer plasma to another tube without picking RBC. Centrifuge at 2500rpm for 15min(Hard spin)to get platelet pellet. The addition of 2-3 drops of thrombin, Collagen, or calcium chloride is optional to enhance the activation. Another optional step is to dip the bottom of the tube containing PRP in liquid nitrogen for 1 minute. Thaw by rolling in the palm. Repeat this three times to disrupt the platelets to release growth factors.

STEM CELL THERAPY

Ovarian rejuvenation with Autologous Stem Cell Transplant (ASCT) is a good option for poor responders, POI, and DOR. This helps in the regeneration of follicles and improves the oocyte quality and ovarian reserve in turn reducing the need for Donor oocytes in ART. Different types of stem cells from various sources have been studied as regenerative medicine is emerging. Among these, M**esenchymal stem cells (MSCs)** have been the most widely studied and used. The Mesenchymal stem cells can be derived from human and murine amniotic fluid, umbilical cord, human menstrual blood, adipose tissue, and Bone marrow. They have properties like proliferation, differentiation to different lineages, and self-renewal.[7] The MSC has the advantage of less immunogenicity and immunomodulatory properties.[8] Stem cells inhibit apoptosis through various mechanisms like secretion of stanniocalcin-1 and cell cycle arrest through ECM Dependent, FAK-AKT signaling pathway, reducing levels of Baz, p53, caspase-3, and Bcl2.[9]

Recovery of damaged ovarian function after stem cell therapy is complex. The transplanted stem cells differentiate into granulosa-like cells more easily than other cells like theca cells, corona radiata cells, and vascular endothelial cells.[10,11]

Bone Marrow-derived stem cells (BMDSC) secrete growth factors, hormones, and chemokines which also influence the adjacent cells referred to as Paracrine signaling. This helps in improving the ovarian microenvironment or Ovarian niche for the recovery of damaged tissues.[12]

BMDSCs selectively migrate to the defective microenvironment and under the influence of various factors repair the niche that is Homing Phenomenon. They help in the recovery of histological and endocrine function.[11]

They express genes relative to VEGF, FGF-2, and IL-6 thus stimulating neovascularization and improving blood supply to the primordial follicles.[13]

Preparation of Autologous bone marrow-derived stem cells

About 120-150ml of bone marrow aspiration is taken from the posterior superior iliac spine under local anesthesia using a Jamshidi needle and heparin prewashed 20ml syringe. 15-16ml BMDSC is extracted with the automated cell separator using optical sensor technology, centrifugation, and sedimentation. The final stem cell concentration is about 5-13 million cells/ml and is patient-dependent.

The use of PRP to improve ovarian function was started in Greece by Pantos et al in 2016.[14]

Hosseini et al studied the effects of Platelet-Rich Plasma(PRP) on the survival and growth of isolated early human follicles in a three-dimensional culture system and concluded that it supports the viability and growth of isolated early human preantral follicles in vivo.[15]

In multiple case series studies it is documented that after PRP treatment, FSH levels have decreased compared to pre-treatment levels. It is also noted that the menstruation is restored and subsequently better oocyte retrieval and cryopreserved embryos.[15,18]

Sillie et al in a case series illustrated the effectiveness of PRP in four DOR patients. After Ovarian rejuvenation with PRP, they had a minimum of one blastocyst for cryopreservation and reduced FSH levels. AMH levels were not significantly affected.[16]

In a study, by Petryk et al, 38 infertile women with DOR and two or more failed IVF cycles received intraovarian PRP. After the procedure, a significant decline in FSH and LH levels was noted. A slight increase in AMH level and about 26% (10/38) of pregnancy rate was observed.[17]

In another case series, 311 women with POI and elevated serum FSH levels PRP treatment increased the antral follicle count (AFC) and AMH.

23 women become pregnant spontaneously, and 16 live births. Among women undergoing IVF, thirteen pregnancies and nine live births were recorded. In total, 25(8.0%) women had a live birth and another 25 (8.0%) had cryopreserved embryos.[18]

Edessy et al. studied Ovarian rejuvenation with Autologous Bone marrow-derived stem cells in 10 POI women with positive results i.e. return of menses in two patients and one ongoing pregnancy, with one live birth.[19]

In 2018, Tandulwadkar and Gupta et al. reported the world's first successful case of Stem cell therapy in a 45-year-old female who had a successful live birth.[20]

In a comparative study between ovarian rejuvenation with PRP and ABDSC done by N. Singh et al, significant improvement of AFC was noted in the PRP group with not much difference in serum FSH level, AMH level, and estradiol level post-treatment.[21]

Sunita.T et al in the study used both Autologous bone marrow-derived stem cells and platelet-rich plasma for ovarian rejuvenation in poor responders. They concluded that combined therapy is safe in optimizing the recruitment of already existing primordial follicles and further improves the number and quality of embryos in poor responders.[22]

KEY POINTS

1. With the increasing age of marriage IVF clinics are witnessing more women with age-related decline in Ovarian reserve coupled with other causes of decreased ovarian reserve.
2. Couples with diminished ovarian reserve have a desire to have their biological child hence bringing forth a need for rejuvenating ovarian function.
3. Ovarian rejuvenation can be accomplished by injecting PRP or Stem cells into the ovaries.
4. Ovarian rejuvenation with PRP and stem cell therapy is safe.
5. The development of primordial and primary follicles to the preantral stage can be enhanced by the use of ovarian PRP.
6. Stem cell injection prevents granulosa cell apoptosis thereby improving ovarian function.
7. Both modalities have different mechanisms of action to restore ovarian function.
8. Key ovarian reserve parameters like FSH, AMH, and antral follicle count have improved after these ovarian rejuvenation procedures.
9. Spontaneous resumption of the menstrual cycle has been observed.
10. The incidence of spontaneous pregnancies has increased according to various studies.
11. Ovarian rejuvenation with PRP and stem cell therapy have shown improved results in ART procedures like increased number and quality of oocytes retrieved and embryos formed in patients with decreased Ovarian reserve and POI.
12. Ovarian rejuvenation brings hope to couples with decreased Ovarian function who want their biological child and have the option to use their gametes vs. donor eggs.

CONCLUSION

Ovarian PRP and Stem Cell injection are new modalities to restore Ovarian function and have shown promising results in regularising menstrual function; Improving the Ovarian reserve parameters as well as increasing pregnancy rates.

More studies need to be done to establish their role in increasing pregnancy rates and live birth rates. Also, studies should be done to compare their efficacy and their combined use in the future.

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Male Infertility – Investigations and Treatment

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INTRODUCTION

Infertility affects 15% of couples making almost one in six childless. Males are solely responsible in 20% of cases and contributory factors in another 30 to 40% of infertility cases. Male infertility is defined as the inability of the male to make his female partner pregnant even after one year of unprotected intercourse.[1]

Discussion

Causes of male infertility can be classified as

- Pretesticular – hypogonadotropic hypogonadism, chromosomal disorders, coital disorders such as retrograde or anejaculation, ED.
- Testicular – testicular malignancy, cryptorchidism, varicocele, epididymal dysfunction, various drugs and toxins.
- Posttesticular – congenital absence of vas deferens, post vasectomy, lesions of the seminal tract, disorders of ejaculation secondary to TURP, RPLND, rectal surgeries.

Evaluation

Purpose of male partner evaluation:

- To look for any cause of male factor infertility.
- To look for any treatable cause of infertility
- To determine any possibility of an assisted reproduction technique

Evaluation includes comprehensive medical and sexual history, history of any addiction, occupation, drug history, surgical history, comorbidities, and treatment history.

Physical examination to look for any possible signs of endocrinopathy, skin, or hair growth pattern.

Genital examination to look for any hypospadias, phimosis, or peyronie's disease.

Bilateral testicles and vas deferens are examined and compared.

INVESTIGATION

Semen analysis –most important first-line investigation for male infertility. At least two samples should be collected three weeks apart with at least one day of abstinence.

Reference limit

pH	:	> 7.2
Sperm concentration	:	12 -16 million per ml
Volume	:	1.5 ml
Total sperm count	:	33 – 46 million per ejaculate
Motility	:	40%
Progressive motility	:	32%
Vitality	:	58% live.
Morphology	:	4%
Liquefaction	:	20 to 30 minutes.

Terminology related to abnormal semen quality:

- Azospermia – no spermatozoa in ejaculate.[2]
- Asthenozoospermia – less than 32% progressively motile.
- Oligozoospermia –less than 15 million per ml, sperm concentration.
- Pyospermia – leucocytes of more than one million per ml.
- Teratozoospermia - <4% morphologically normal spermatozoa.

Various semen assays:

Antisperm antibodies are usually indicated in cases with isolated asthenozoospermia having normal sperm concentration

Chromosomal testing and genetic screening are indicated with oligozoospermia and azoospermia. The most common disorders associated are Y chromosome micro divisions, and congenital absence of vas due to CFTR gene mutation

so genetic testing consists of karyotyping, CFTR, and Y chromosome testing for microdeletions.

Hormonal testing – The hormone milieu of the testis plays a crucial role in spermatozoa formation. The cornerstone of hormonal control lies in the hypothalamic-pituitary axis.

The hypothalamus secretes GnRH which feeds the anterior pituitary gland resulting in the release of LH and FSH from the anterior pituitary. LH stimulates testosterone production from Leydig cells.FSH is crucial for spermatogenesis maintenance.

The lab evaluation panel includes FSH, LH, testosterone, and prolactin.

Approach to some common clinical scenarios:

- Low testosterone and increased FSH and LH – primary hypogonadotropic hypogonadism; karyotype to be done.
- Low testosterone and normal or low FSH and LH – suggest secondary hypogonadism; prolactin to be checked.
- Normal testosterone, LH, and FSH – If there is azoospermia, it indicates obstructive cause. Also look for B/L vas deferens in those cases, if absent, it may indicate CFTR gene mutation.
- Normal testosterone and LH with high FSH indicate primary spermatogenic failure if azoospermia exists.
- Postejaculatory urine analysis in semen volume less than one ml.

Scrotal USG was done to identify pathology in 38% of infertile males. Preferred as a painless, noninvasive modality. Can diagnose other pathologies like varicocele, spermatocele, absence of vas, testicular mass, ejaculatory duct cyst, or prostatic cyst

Testicular biopsy – usually done in suspected ductal obstruction cases presenting with azoospermia with normal size testis and normal hormone level.

Trans-rectal ultrasound to rule out any ejaculatory duct obstruction should be done along with post-ejaculatory urine analysis and low semen volume.[3]

Vasography – useful adjunct in azoospermia or severely oligospermia males with mature sperm to evaluate vas patency.

Postcoital test – indicated in cases of unexplained infertility. It is done by examining cervical mucus for viable sperm 8 hours after intercourse and is usually done 2 days before ovulation.

Other tests can be done if the postcoital test is normal –

- Sperm vitality staining
- Inhibin B level
- Acrozome, capacitation reaction

Semen analysis results with suggested treatment

Normospermia – patients will either have idiopathic male infertility or infertile females. ART can be considered.

Asthenozoospermia – anti-sperm antibody should be checked especially if associated with increased agglutination, ART can be considered.

Low semen volume – retrograde ejaculation and ejaculatory duct obstruction are possibilities and post ejaculatory urine analysis should be done.

Oligospermia/azoospermia – hormone levels are checked. If vas is present, testicular volume is normal, possibly obstructive azoospermia. The preferred treatment is vasovasostomy/vasoepididymostomy, if fails then ART should be considered.

If bilateral absence of vas, then ART is to be considered.

TREATMENT APPROACH

Healthy lifestyle changes are recommended.

- Stop smoking or alcohol intake.
- Weight loss if obese
- Increase exercise
- Decrease mental stress
- Decrease recreational drug abuse
- Avoid artificial lubricant during intercourse

Medical Treatment

Following treatment modalities have shown some beneficial effects on sperm quality or male infertility-

L-Carnitine – Amino acid found in epididymis, known to increase fatty acid transport into sperm mitochondria. Increased sperm motility, morphology, maturation, and decreased apoptosis

Antioxidants – for reduction of oxidative stress in semen. Antioxidants include selenium, zinc, and folic acid. Coenzyme Q10 taken for three months has shown improvement in semen parameters.

Other treatment options with controversial efficacy:

Gonadotrophic therapy – a combination of HCG, LH, FSH

Treatment in males with idiopathic infertility is unclear. They have better results when used to correct pituitary and hypothalamic disorders.

Congenital hypogonadotropic hypogonadism - hcG or exogenous testosterone

Adult onset hypogonadotrophic hypogonadism – hcG 2000 to 5000 IU thrice weekly.

Non – Non-responders – hcG or pure FSH 75 to 100 iu thrice weekly.

Eugonadotrophic hypogonadism presenting with Severe oligospermia and Low testosterone – treated by aromatase inhibitor.

Hypogonadotropic hypogonadism:

IVF with ICSI with preliminary genetic evaluation.

Surgical Treatment

The urologist can be part of a multi-professional reproductive technique in the assisted reproduction unit being responsible for diagnosis, counseling, and providing medical or surgical treatment wherever possible as well as sperm retrieval from the epididymis or testicle. Two breakthroughs in the area of infertility were the development of microsurgery for the reconstruction of the reproductive tract. Second was the development of ICSI and the demonstration that spermatozoa retrieved from the testes or epididymis were capable of fertilization and pregnancy.[4]

Ejaculatory Duct Cyst/ Prostatic Duct Cyst Resection:

Midline prostatic and ejaculatory duct cysts are present in 10% of infertile males. A male presenting with severe oligozoospermia, low ejaculate volume, normal hormonal screening, and dilated seminal vesicle on transrectal ultrasound should be suspected. Cysts can be managed with either transurethral resection or cyst puncture. Transurethral resection is considered the most definitive option with improvement in semen quality in 50% of cases.

Varicocelectomy:

Varicocele can be identified in up to 35% of the male population with infertility complaints. Only indicated in infertile males with pathological semen levels having grade 3 varicocele usually results in improving semen parameters in 60 to 70 % of cases. Among cases with subclinical varicoceles who are diagnosed with infertility were more likely to have bilateral disease, lower testicular volumes, and higher average scrotal temperature. Varicocele is treated by open or lap technique – retroperitoneal approach, inguinal approach, subinguinal approach. However, surgery is not recommended in cases with severe oligozoospermia or high FSH concentration as these features suggest sperm cell damage making the patient unlikely to see any improvement in the fertility.

Transurethral resection of ejaculatory duct:

Patients with ejaculatory duct obstruction detected on transrectal ultrasound are likely to benefit from transurethral resection of the ejaculatory duct, which is done by verumontanum resection.

Vasovasostomy and vasoepididymostomy:

They are advanced microsurgical procedures done for patients with obstructive azoospermia secondary to bilateral epididymal or vas obstruction together with normal testicular size and hormonal levels. The improved fertility rate has been noted with vasovasostomy compared to vasoepididymostomy and if the original obstructive event was surgical. Men with increased FSH may require ART over and above this procedure to achieve pregnancy. However, varicocele repair and vasovasostomy should not be simultaneously performed owing to the increased risk of vascular compromise of the testicle.

Sperm retrieval techniques:

Azospermia is found in 1-3% of the male population and almost 10% of infertile males.[5] Two clinical. Two different clinical situations exist – obstructive azoospermia (OA) and non-obstructive azoospermia(NOA). In both OA and NOA pregnancy may be achieved through IVF associated with ICSI. Several methods have been developed for sperm retrieval from the testicle and epididymis.[6] Either Percutaneous epididymal sperm aspiration (PESA) or Microsurgical epididymal sperm aspiration (MESA) can be used to retrieve sperm from epididymis in cases of obstructive azoospermia. Testicular sperm aspiration (TESE) can be used to retrieve sperm from the testis both in cases of OA who fail with PESA as well as those with NOA.[7]

Testicular sperm extraction(TESE) and more recently microTESE is indicated for men with NOA.

Intrauterine insemination (IUI):

An assisted reproduction technique where semen is artificially instilled into the female uterus. Most useful when the postcoital test shows no sperm or significant abnormal sperm parameters. In unexplained or mild male factor infertility, three to four attempts of IUI are often done before switching to a further expensive modality like IVF. Intrauterine insemination is not recommended when sperm are dead. Abnormal sperm tests such as acrosomal reaction or sperm penetration assay suggest IVF with ICSI should be used. As a general rule, a total motile sperm count of one million is required for successful intrauterine insemination.

Invitro fertilization and ICSI:

It can be used when IUI with ovarian stimulation has failed or in cases in which simpler techniques cannot be used such as bilateral tubal disorders. It involves female egg fertilization outside her body. Around one lakh sperms are added for each egg retrieved either through ejaculation or direct testicular extraction. A minimum of fifty thousand to five lakh motile sperm are needed for IVF. Otherwise, ICSI is recommended for those with a lower count. The pregnancy rate is 10 to 45%.[8]

ICSI involves the use of a microscope to inject single sperm retrieved from the male partner directly into the egg of the female partner and fertilized eggs are then implanted into the uterus. The overall fertilization rate is around 60%. IVF with ICSI is preferred in cases of severe male factor infertility when other measures have failed.

CONCLUSION

Although many cases of male infertility are secondary to primary testicular failure, some can be treated medically. So, it is prudent to identify and treat the pathology early or make early reference to the appropriate centre. Infertility is seen as a social stigma and proper counseling of patients and relatives should be done.

KEY POINTS:

1. A comprehensive history including sexual history and physical examination of the body habitus, hair distribution, and male genitalia to be done.
2. At least 2 separate semen analyses are required, optimally one month apart.
3. Hormonal screening including FSH, LH, testosterone, estradiol, TSH, and prolactin is required.
4. A scrotal ultrasound is to be done.
5. Genetic screening is required for patients with severe oligozoospermia.
6. Treatment depends upon the overall sperm count and the cause of the infertility.

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Obituary

Dr. Daljit Kaur Uppal

(1949 – 2024)

Dr. Daljit Kaur Uppal, beautiful person inside out. Born in 1949, she did her graduation from Amritsar Medical college and post graduation from PGI Chandigarh. A clinician par excellence she spent her initial years at R K Puram CGHS dispensary followed by Safdarjung hospital where she worked till retirement. She was the founder member of the FOGsd society (Forum of obstetricians and gynaecologist of south Delhi). A very brave lady, she passed away peacefully in the presence of both her children. She is survived by husband Dr. Sarvajit Singh Uppal, daughter Dr. Prerna and son Dr. Simardeep. We will cherish her life and the wonderful memories she created with all of us. She will always be a part of our prayers and memories.

On behalf of all AOGD members we express our heartfelt condolence to the family and pray to God to give them strength to bear the loss.

AOGD FAMILY

Surrogacy Act

Dr. Leena Wadhwa[1], Dr. Pooja Gupta[2]

Professor & Head of Department Senior IVF, Consultant Obstetrics & Gynaecology, ESIC Medical College and Hospital, Rajasthan[1]
Consultant, Origin Fertility & IVF, New Delhi[2]

The word SURROGATE is derived from the Latin word '*surrogatus*', which means a "substitute or appointed to act in the place of."

Surrogacy refers to an agreement whereby one woman bears and gives birth to a child for an intending couple when pregnancy is either medically impossible or it is considered very risky for the mother's health, with the intention of handing over such child to the intending couple after the birth.

TYPES

(A) Traditional surrogacy- impregnation of the surrogate naturally or artificially, and the resulting child is genetically related to the surrogate.

(B) Gestational Surrogacy - pregnancy occurs due to the transfer of an embryo created by in vitro fertilization such that the resulting child is genetically unrelated to the surrogate. This can be further classified as

1. Commercial surrogacy-

   This means commercialization of surrogacy service, trading the services of surrogate motherhood by way of giving payment, reward, benefit, fees, remuneration, or monetary incentive in cash or kind, to the surrogate mother or her dependents or her representative, except the medical expenses and such other prescribed expenses incurred on the surrogate mother and the insurance coverage for the surrogate mother.

   Commercial surrogacy has been banned in India as per new ART Regulations in 2021. Some people, Governments, and religious groups questioned the ethics of involving money. This had also spiraled into unethical practices, putting the lives of both surrogate woman and their babies at risk.

2. Altruistic surrogacy –

   This means the surrogacy in which no expenses, fees, remuneration or monetary incentive, or any charges of whatever nature, except the medical expenses and such other prescribed expenses incurred on the surrogate mother and the insurance coverage for the surrogate mother, are given to the surrogate mother or her dependents or her representative. This is allowed as per new ART regulation vide Notification no. S.O. 292(E), dated 20th January 2021, Gazette of India, Extraordinary, Part II, sec. 3 (ii).

HISTORY

Commercial surrogacy has been legal in India since 2002. In 2005 the first effort to regularize surrogacy in India was made by the Indian Council for Medical Research (ICMR) working under the Ministry of Health and Family Welfare.

In August 2009, the Law Commission of India specifically reviewed the surrogacy law.

Law Commission of India has submitted the 228th Report on "Need for Legislation to Regulate Assisted Reproductive Technology Clinics as well as Rights and Obligations of Parties to A Surrogacy"[1]

In the year 2010, the Indian Council of Medical Research (ICMR), under the Ministry of Health & Family Welfare, the Government of India revised the ART Guidelines including for surrogacy. As per these guidelines, surrogacy was commercially allowed to help infertile patients. The guideline proposed to have a written agreement for surrogacy between the prospective surrogate and the ART clinic explaining the methods of treatment.[2]

SURROGACY ACT 2016

On 24th August 2016, the Union cabinet approved the Surrogacy (Regulation) Bill, 2016 and restricted surrogacy to Indian married infertile couples only and barring persons of Non-Indian Origin, Non-Resident Indians along with Overseas Citizens of India (OCI) for commissioning surrogacy in India. It allows ethical altruistic surrogacy to married infertile couples only.[3]

SURROGACY ACT 2021

The Rajya Sabha made a committee for discussion of the Surrogacy (Regulation) Bill 2019 with various stakeholders

and the conclusion of which led to some more amendments, culminating in its passage into law on December 25, 2021.

On January 25th, 2022, the new Surrogacy (Regulation) Act, 2021, came into force. The amended act exclusively permits charitable surrogacy, preventing those with financial means from abusing and taking advantage of the surrogacy option. It prohibits commercial surrogacy, as well as the trade of human gametes and embryos. The Surrogacy (Regulation) Rules, 2022 were published in the Gazette of India, Extraordinary, Part II, Section 3, sub-section (i) vide G.S.R. 460 (E)dated 21st June 2022 subsequently amended vide notification number vide G.S.R. 772 (E) dated 10th October 2022, G.S.R. 179 (E) dated 14th March 2023 and G.S.R. 415(E) dated 8th June, 2023.[4]

Surrogacy Clinics: means clinic, Centre or laboratory, conducting assisted reproductive technology services, in vitro fertilization services, genetic counseling center, genetic laboratory, Assisted Reproductive Technology Banks conducting surrogacy procedure or any clinical establishment, by whatever name called, conducting surrogacy procedures in any form.

Registration

- Surrogacy clinics can apply for registration through the National ART & Surrogacy Registry portal.
- The PDF printout of the filled-in application form duly signed by the authorized signatory/ competent authority on behalf of the bank may be submitted electronically or by registered post or in person to the Appropriate Authority, through the office of Additional Chief Secretary (Health)/ Additional Secretary (Health)/ Principal Secretary (Health)/ Secretary (Health)/ Joint Secretary (Health) of the respective State/ UT Government.
- Every application for registration shall be accompanied by an application fee of: - Rupees 2,00,000, free for government organizations.
- Registration is valid for 5 years.

The Surrogacy Regulation Act, 2021 highlights:-

Intending Couple, Surrogate Mother and Intending Woman: Definitions and Eligibility

Surrogate Mother: a woman who agrees to bear a child (who is genetically related to the intending couple or intending woman) through surrogacy from the implantation of the embryo in her womb and fulfills the conditions (eligibility criteria) as provided in sub-clause (b) of clause (iii) of Section [4]

- Willing ever married with a child of her own
- Age 25-35yrs on the day of implantation
- Willing woman approved by appropriate authority
- Registered medical practitioner certifies that she is Medically and psychologically fit for surrogacy.
- Never been a surrogate before
- Not more than three times for the same couple
- Husband's consent
- Eligibility certificate by Appropriate authority
- Forbidden from providing her own gametes

Intending Women: Indian woman who is a widow or divorcee between the ages of 35 to 45 years and who intends to avail the surrogacy.

Intending Couple: A legally married Indian man and woman, the man shall be between the ages of 26-55 years and the woman shall be between the ages of 23-50 years, and shall not have any previous biological, adopted, or surrogate child.

Medical conditions necessitating surrogacy-

- She has no uterus or missing uterus or abnormal uterus (like hypoplastic uterus or intrauterine adhesions or thin endometrium or small uni-cornuate uterus, T-shaped uterus), or if the uterus is surgically removed due to any medical conditions such as gynecological cancer.
- Intended parent or woman who has repeatedly failed to conceive after multiple In vitro fertilization or Intracytoplasmic sperm injection attempts. (Recurrent implantation failure)
- Multiple pregnancy losses resulting from an unexplained medical reason. Unexplained graft rejection due to exaggerated immune response.
- Any illness that makes it impossible for a woman to carry a pregnancy to viability or a life-threatening *pregnancy.*

Prerequisites

As per the Act, only those cases fulfilling the following situations are eligible for taking use of surrogacy procedures when there is a medical indication. The District Medical Board must issue this indication certificate in favor of the commissioning party when -

1. The intended parents are of Indian origin.
2. The intended mother is a divorcee or widow.
3. The surrogacy is for charitable purposes.
4. It is not being done for financial gain.

Checklist for Undergoing Surrogacy

1. The intending couple has a certificate of essentiality (Form 11) issued by the appropriate authority, after satisfying itself, for the reasons to be recorded in writing, about the fulfillment of the following conditions, namely:
   (a) A certificate of a medical indication in favor of either or both members of the intending couple or intending woman necessitating gestational surrogacy from a District Medical Board(medical board under the Chairpersonship of Chief Medical Officer or Chief Civil Surgeon or Joint Director of

Health Services of the district and comprising of at least two other specialists, namely, the chief gynecologist or obstetrician and chief pediatrician of the district). (Form 12)

(b) Order concerning the parentage and custody of the child to be born through surrogacy, by a court of the Magistrate of the first class or above on an application made by the intending couple or the intending woman and the surrogate mother, which shall be the birth affidavit after the surrogate child is born. (Form 13)

(c) An insurance coverage of such amount and in such manner as may be prescribed in favor of the surrogate mother for a period of thirty-six months covering postpartum delivery complications from an insurance company or an agent recognized by the Insurance Regulatory and Development Authority established under the Insurance Regulatory and Development Authority Act, 1999 (41 of 1999)

2. Eligibility certificate for Surrogate mother issued by the appropriate authority on fulfillment of the eligibility criteria (form 17 b) along with a certificate of medical and psychological fitness (form 14)

3. An eligibility certificate for an intending couple is issued separately by the appropriate authority on fulfillment of the eligibility criteria as mentioned above. (Form 17) Eligibility certificate for intending women (Form 17 a).

- **Number of embryos to be implanted -** The gynecologist shall transfer one embryo into the uterus of a woman during a treatment cycle. However, only in explainable circumstances up to three embryos may be transferred.
- **Withdrawal of consent**
- The surrogate mother shall have the option to withdraw her consent for surrogacy before the implantation of the embryo in her womb as specified in Form 15.
- **Medical termination** - No person, organization, surrogacy clinic, laboratory, or clinical establishment of any kind shall force the surrogate mother to abort at any stage of surrogacy except in such conditions as may be prescribed. The surrogate mother may be allowed for abortion during the process of surrogacy in accordance with the Medical Termination of Pregnancy Act, of 1971.
- **Attempts -** The number of attempts of any surrogacy procedure on the surrogate mother should not be more than three times in the same couple.
- **Complaints** - The format for making a complaint to the appropriate authority against a surrogacy clinic is specified in Form 16.
- **Maintenance of records**- Surrogacy clinics shall preserve all documents for a period of 25 years and if required beyond this period after seeking due permission from the National Board. At least one copy of each of the Act and these rules shall be available on the premises.

OFFENCES & PENALTIES

1. **Prohibition of commercial surrogacy, exploitation of surrogate mothers and children born through surrogacy** - punishable with imprisonment for a term which may extend to ten years and with a fine which may extend to ten lakh rupees.
2. **Punishment for contravention of provisions of the Act-** punishable with imprisonment for a term up to five years and with a fine which may extend to ten lakh rupees.

   In case of subsequent or continuation of the offense referred to in, the name of the registered medical practitioner shall be reported by the appropriate authority to the State Medical Council concerned for taking necessary action including suspension of registration for a period of five years.
3. **Punishment for not following altruistic surrogacy**- punishable with imprisonment for a term which may extend to five years and a fine which may extend to five lakh rupees for the first offense and for any subsequent offense imprisonment which may extend to ten years and a fine which may extend to ten lakh rupees**.**

RECENT AMENDMENTS

1. The first amendment to the Rules was vide notification dated 10 October 2022 Amendment requires the intending couple to purchase insurance coverage for 36 (thirty-six) months and that such insurance coverage should be guaranteed by signing an affidavit. Earlier, the provision stated that this affidavit needs to be sworn by signing an affidavit before the Metropolitan Magistrate or Judicial Magistrate of the First Class.

   The 2022 Amendment allowed it to be sworn before either of the additional two classes of authorities, i.e., Executive Magistrate or Notary Public promoting flexibility to the intending couple and making way for a quicker process of surrogacy application**.**
2. The second amendment to the Rules has come in recently vide notification dated 14 March 2023 ("2023 Amendment"). It disallows for intending couples to commission surrogacy with donor gametes.

   A. Couples undergoing Surrogacy must have both gametes from the intending couple & donor gametes are not allowed.

   B. Single woman (widow/divorcee) undergoing Surrogacy must use self-eggs and donor sperm to avail surrogacy procedure**.**
3. Third Amendment –June 2023 vide notification dated the 8th June 2023

   with the Acts/Rules/Instructions/Guidelines being followed by the Ministry of Home Affairs from time to time subject to fulfillment of various criteria as per

the Surrogacy (Regulation) Act, 2021". The following clause shall be inserted, namely: -Couple of Indian Origin means the couple where both husband (male) and wife (female) are Overseas Citizens of India cardholders in accordance with the Acts/Rules/ Guidelines being followed by the Ministry of Home Affairs.

4. Recent amendment in February 2024

   In case when the District Medical Board certifies that either husband or wife constituting the intending couple suffers from a medical condition necessitating the use of donor gamete, then surrogacy using donor gamete is allowed,"

   The surrogacy using donor gamete is allowed subject to the condition that the child to be born through surrogacy must have at least one gamete from the intending couple, This means if both the partners have medical problems or are unable to have their gametes they cannot opt for surrogacy.

   "Single women (widow or divorcee) undergoing surrogacy must use self-eggs and donor sperm to avail surrogacy procedures,"

Limitations and PIT Falls in Surrogacy Act 2021 - Need of Amendment

- Depriving Plebeians of Their Reproductive Autonomy (based on strict age criteria)
- The glass ceiling "women's rights" -prevents unmarried women from availing of the services of surrogacy.
- Excluding live-in relationships from the scope.
- Long-term health implications on the surrogate mother and the fetus: an unsettled debate-. If in any case, the fetus is affected due to an accidental or intentional consumption of drugs or, the risk of acquiring venereal disease by the surrogate, the act has no provision for consequences on her.
- Unseen mental health implications.
- No provision to compensate for the loss of wages of a surrogate mother.
- Excludes certain sections of society, such as LGBTQIA+ individuals, and single fathers.
- Increasing time to conception and creating a backlog of infertile couples who are waiting for someone to help them altruistically.

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4. Ministry of Law and Justice, Government of India. The Surrogacy (Regulation) Act. (2021). Accessed: April 19, 2023: https://dhr.gov.in/document/acts-circulars/surrogacy-regulation-act-2021.

Awards and Prizes

Quiz Competition in The FOGSI Food and Drug & Medico Surgical Equipment Committee National Conference held at Dehradun, from June 14-16, 2024

- *First prize - Dr. Sreeba Balakrishnan ABVIMS & Dr. RML Hospital, Delhi) and Dr. Pragya Mishra (ABVIMS & Dr. RML Hospital, Delhi)*
- *Second Prize - Dr. Sakshi Bajaj (AIIMS, Delhi) and Dr. Neeraja G (BSA Hospital, Rohini, Delhi)*

Social Impact of Infertility on a Couple: How to Comfort and Counsel

Dr. Ram Pratap Beniwal[1], Dr. Priyanka[2]

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Department of Psychiatry & Drug De-addiction, Centre of Excellence in Mental Health,
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INTRODUCTION

Infertility is a complex health problem that involves both disturbances of physical and mental health. Infertility impacts various facets of an individual's life, including familial, financial, emotional, and social problems. World Health Organization (WHO) states, "Health is a state of complete physical, mental and social well-being"; infertility is one such withering entity that affects all these domains to varying degrees. Accordingly, it becomes essential that we talk about infertility and its pervasive impact on mental and social health. Infertile couples or individuals frequently demonstrate signs of stress, anxiety, depression, financial hardships, guilt, fear, loss of social status, despondence, and social labeling. Due to the stigma associated with both infertility and psychological disorders, the couple usually conceals such issues. The lack of awareness among healthcare professionals also contributes to this inadvertency. Hence making it difficult for healthcare professionals to identify and correctly evaluate the psychological state of infertile couples. This could further adversely affect a couple's quality of life and infertility management. By fostering an environment of openness and understanding, mental healthcare professionals can better support these patients through the emotional challenges of infertility and improve further prognosis.

Psychological factors and infertility: a two-way relationship

Evidence is available to present a model whereby infertility causes many social and psychological problems, and social issues complicate the infertility problem. Failure to accomplish the reproduction function leads the couple to feel like a loser and idler. By negatively affecting social life, mood, marriage life, sexual life, plans, self-respect, body image, and life quality of couples, infertility then turns into a complex life crisis. For a woman, childlessness is associated with infertility (functional disorder), loss of control (my body rebelling against my will), psychological void (unfulfilled maternal instinct), feeling outcast from the female community, feeling worthless, loneliness (lack of emotional support of the child), absence of social security (nobody to look after them in old age), unmet social role (mother, pregnant woman, postpartum period, mother-in-law), and lower self-esteem. Infertility is still considered as a woman's fault or lack of womanhood, or a man's weakness in impregnating women in many parts of India.

The causal factors of infertility are not limited to medical factors but extend to psychological and social aspects, too. Among some of the potential underlying causes with psychogenic roots are fear of having a bad body shape due to pregnancy, fear of losing her life or the baby during delivery, or fear of failing as a good mother. Among men, impotence and ejaculation problems are the root causes of psychological infertility. A significant part of impotence could be related to psychological causes. Most of the time, past psychological traumas, nutritional disorders, childhood diseases, and over-affectionate and protectionist mothers are among the initiative factors of psychological impotence.

Impact of Sexual Infertility Stress on infertile couples

Sexual infertility stress has been defined as loss of enjoyment of sexual relations, feelings of pressure to schedule sexual relations, and loss of sexual self-esteem.[1] Among men, sexual infertility stress is often connected with feelings of reduced masculinity, performance anxiety, and a perceived threat to manhood. The presence of 'state anxiety' (anxiety triggered by a particular problem or situation) in couples or individuals pursuing assisted reproductive technology is a predictor of treatment success. Peterson et al. reported that men and women who showed more significant anxiety at the start of treatment may have increased levels of sexual infertility stress. Physicians should provide primary education regarding the relationship between anxiety and sexual infertility stress and refer these couples to mental health professionals for management.[2]

Gender differences

Numerous research on gender variations in infertility have found high levels of stress, anxiety, and depression. Compared to infertile men, infertile women experience greater strain and distress. The spouses of infertile men had

higher levels of stress, worry, and depression than did the spouses of infertile women.[3] According to studies, women typically have more family and social problems and bear the brunt of infertility, even when the infertility is caused by male factors.[4]

Societal and Health Implications

Infertility is a worldwide public health issue affecting an individual's personal, social, and economic life and the family as a whole. A considerable proportion of infertility is a result of preventable factors, such as smoking, sexually transmitted infections, pregnancy-related infection or unsafe abortion, and environmental contaminants. The WHO has presented the consequences of infertility for infertile people using a diagram shown in Figure 1. The diagram reported that the consequences of infertility in the developed countries can rarely go beyond the level two of the spectrum. In developing countries, the consequences of infertility are at the level three or higher. A mixed-method study in Rwanda reported that if women are unable to become pregnant, husbands have a right to refuse to provide food and clothing for their wives. The in-laws also refuse to give any inheritance to infertile women in the death of their husband.[6]

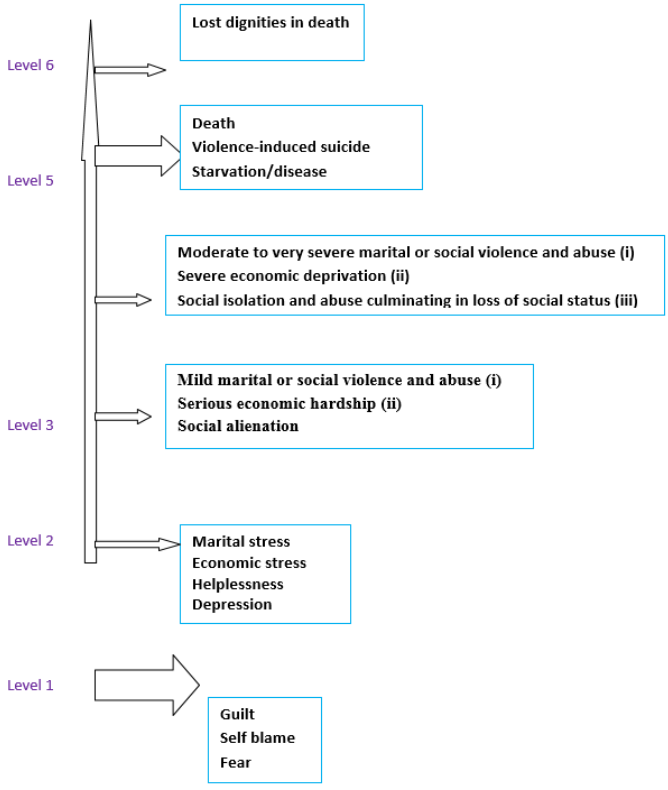

Fig1: Continuum of the consequences of infertility[5]

The religious aspect of infertility

Many religions and faiths place a great emphasis on fertility and childbearing. In Islam, the place of motherhood is highly prestigious, and it is believed among Muslims that "Heaven lies at the feet of mothers." Reproduction is highly recommended in Christianity as well. Judaism encourages its followers to procreate, and some Jewish scholars allow using artificial means for this purpose. A study reported that different cultures have the following three ways to deal with infertility: (a) some accept social solutions, such as divorce, polygamy, and adoption; (b) many use medical techniques and medical plants, while (c) in some cultures, resorting to spiritual people and pilgrimage places are chosen.[7]

The treatment-related social aspect of infertility

Concern over the impact of infertility therapies on the health of women and children conceived through them is growing as the usage of these treatments rises globally. Recent studies reported that hyper-stimulation of the ovaries and exposure to excess hormones may increase the risk for gynecological and breast cancers, but findings are mixed.[8] Women who conceive by infertility treatment are also at greater risk of multiple births and often conceive at older ages, which increases the risk for pregnancy complications and adverse birth outcomes.[9] A quantitative study revealed that one of the most stressful factors for infertile women is going through infertility treatment itself.[10] Therefore, women may be prone to emotional responses, such as enhanced anxiety or depression, due to invasiveness or adverse effects of the treatment.

Financial implications

The high cost of evaluation and treatment is one of the biggest obstacles for those who are infertile. Due to the high cost of fertility care, many couples choose to forego appropriate therapy or turn to alternative therapies, some of which may be harmful, ineffective, or cause a delay in necessary medical care.[11] For those who do look for medical care, the financial load may increase the cost of treatments as well as the costs related to fertility care, including missed time from work or travel expenses.

Stigma in an infertile couple

When a person doesn't meet the social expectations of motherhood, they may face intense stigma from both others and themselves. Reproduction is frequently cited by gender norms as a crucial indicator of adult masculinity or femininity. Worldwide, the finding across cultures is that failure to reproduce may be interpreted by oneself and others as a failure to be a "man" or a "woman".[12]

In societies with a high prevalence of infertility and the stigma associated with it, the perception or fear of infertility may also be high. All the women, regardless of age, educational level, or employment status, had experienced forms of stigma. Mumtaz. et al. 2013 stated that women perceived more stigma than men and that being stigmatized was more painful than being infertile. Men also face stigmatization in the form of humiliation, and society questions their manhood. Furthermore, most individuals do not like the term "infertile". Psychologists believe that

for such people, titles and labels should not be used that imply a flaw (like using child-free instead of childless).[13]

Marital dissatisfaction

Marriage is often viewed not just as the joining of two individuals but as the joining of two families, with a stated outlook that the couple will continue the family pedigree. Due to childlessness (primary infertility), the sexual relationship becomes just grueling work as they lose their pleasure due to conflict and pressure of conceiving a child, resulting in marital satisfaction. Moreover, less frequent sexual intercourse among infertile women leads to the minimal release of endorphins, which is a natural mood booster, thus leading to higher levels of stress.[14]

The marital dissatisfaction due to infertility-related stress can be explained in terms of various endemic factors (family, social, and peer pressure, potential threat of divorce or fear of second marriage by spouse, stigmatization, and loneliness.[15] In other words, we can say that subjecting to pressure partners to achieve parenthood deters their psychological well-being, ultimately impacting their marital satisfaction.

RECOMMENDATIONS

- Infertile women should be counseled by a treating medical specialist regarding reproductive trajectories (Fertility counseling).
- Infertile couples should be guided and counseled to incorporate mental health screening and treatment in their routine checkup.
- Developing infertility-specific tools to measure infertility-related stress and providing counseling to couples on marital relationships and sexuality in infertility is the need of the hour (Psychoeducation).
- Therefore, psychological and marital support during infertility treatment, especially dealing with male factor in infertility considering that sexual and marital stresses play important roles in the course of infertility treatment. (Figure 2)
- Treatment protocol should consider stress both as a cause and as a consequence of infertility and should not commence invasive treatment before verifying whether important levels of both types of stress in any particular case exist and whether these can be reduced.
- A treatment algorithm is advised to follow before start of fertility treatment as per Figure 2.
- Establishing the long-term effect of affectionate expression in the couple for the treatment process could be crucial in tackling this complex life experience [Marital communications skills (Table 1) and marriage counselling].

Diagnosis of Infertility

↓

Establish male and female chronic and acute stress level with validated questionnaire

↓

If over-thresholds: intensive stress reduction techniques for 3 months

↓

Establish stress levels and referral to fertility clinics

↓

Establish male and female chronic and acute stress level with psychological and biological assays

↓

If over-thresholds: intensive stress reduction through psychological and adjuvant/dietry treatment for 3 months

↓

When and if reduction is obtained: initiation fertility treatment with concurrent male and female stress management

Fig. 2: Establishing stress levels before fertility treatment

Table I: Interventions for stress control and fertility treatment

Procedural means	Protocols to include patient selection according to existing chronic stress levels and response to acute stressors Preliminary treatment to reduce anxiety and depression before fertilization cycles are initiated
Psychological means	Cognitive-behavioural therapy Relaxation training Differential orientation as to infertility Fertility sabbatical permit
Technical means	Frozen back-up semen samples taken at low-stress moments outside the fertilization cycle Further refinement of fertilization techniques, such as removal of the acrosome before ICSI
Neurobiological means	Establishing individual baselines and specific stress markers Establishing thresholds for referring Monitoring for stress before and during fertility treatment

CONCLUSION

The biopsychosocial model of illnesses as an alternative to the prevalent biomedical model is a more holistic approach with consideration for psychological, social, and behavioral factors that could contribute to the disease. These factors have an essential role in both the contribution and therapeutics of infertility. Incorporating the psychological and social aspects, when effectively implemented, might prevent problems surrounding infertility (Table 2).

Table 2: Short-term goals for male and female fertility patients

Reduction of feelings of helplessness, through coping with infertility
Changes in sexual behaviour
Modification of negative cognitions as to infertility
Overcoming deficiencies in knowledge about fertility
Improving marital communication skills

Einstein once remarked, "Not everything that counts can be counted, and not everything that can be counted counts." This emphasizes that mere inattention doesn't negate the influence of a factor in an illness. Decades of research have shown the social impact of infertility. Hence, it warrants the clinician's attention to address the social and psychological issues related to fertility.

KEY POINTS

1. Psychological and social factors influence the couple's ability to cope with the infertility more than the problem of infertility itself. These are social or self-stigma, unfulfilled social role and guilt in the couple.
2. The infertile couple might go through the five stages of grief: Denial, anger, bargaining, depression and acceptance, treating physicians can help couple to identify and refer to a mental health professional to timely resolve these stages.
3. Health care professionals can help the couple to find their own best possible adaptation to deal with infertility issues, sometimes finding meaning in new life situation, reformulate their meanings attached to infertility, and psycho-educating them with a practical and scientific explanation.
4. The holistic multi-speciality approach may reduce the treatment dropout and enhance the fertility rate in these couples.

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> LAPAROSCOPIC EXCISION OF SCIATIC NERVE ENDOMETRIOSIS

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Proceedings of AOGD Clinical Meeting - Case Reports
INDRAPASTHA APOLLO HOSPITAL- 28th June, 2024

1. A Rare Case of Post Hysterectomy Vaginal Bleeding

Dr. Anusha Khare[1], Dr. Kiranabala Dash[2], Dr. Shakti Bhan Khanna[3], Dr. Harsh Rastogi[4]

DNB Student[1], Senior Consultant[2,3,4]

Indraprastha Apollo Hospitals

ABSTRACT

Post hysterectomy vaginal bleeding is a rare problem, particularly in women in whom the cervix has been removed with a reported incidence of 0.2-2 %.[1] It Is common to have on and off blood-stained vaginal discharge for several days to several weeks after hysterectomy as stitches dissolve and tissues heal from resolving granulation tissue. Other causes of post hysterectomy vaginal bleeding include atrophic vaginitis, cervical stump cancer, infiltrating ovarian tumors, estrogen secreting tumors from other parts of the body, bladder pathology, endometriosis of vault, vaginal cuff tear secondary to hematoma or infection. We reported a case of 41 years old female, who underwent total abdominal hysterectomy with left salpingo-oophorectomy and right salpingectomy for uterine fibroids and presented with vaginal bleeding, which started after one week and continued for three weeks post-surgery. On examination, the vault looked raw, bleeding was coming through the center of the vault. No pelvic collection was found on ultrasound. After management with Tranexamic acid and broad-spectrum antibiotics, the vault was re-sutured vaginally. The vaginal bleeding restarted after three weeks. CT angiography revealed prominent vascular channels arising from the right internal iliac artery. Super-selective angio-embolization was done. She was symptom free after that.

INTRODUCTION

Post Hysterectomy vaginal bleeding is not a common problem, with a reported incidence between 0.2-2.%.[1] Bleeding per vaginum can happen for a few days post Hysterectomy but persistent vaginal bleeding must be taken care of and the cause should be ruled out. The amount may vary between spotting to heavy bleeding per vaginum, both can be stressful to the patient. Heavy bleeding can also be life-threatening to the patient. Post-operative bleeding can be classified as reactionary (within 24 hrs after surgery), and secondary (between days 3-22 after surgery). Unexpected haemorrhage can arise regardless of route and type of Hysterectomy. Early recognition, proper diagnosis, and prompt intervention are essential strategies for suitable patient outcomes. Reported causes of delayed bleeding are infection, hematoma, granulation tissue formation, vaginal atrophy, vascular malformations, endometriosis, and many others. Bladder and bowel pathologies may cause fistulas resulting in bleeding from vault.[2,3,4] Selective embolization of pelvic arterial vessels has been reported in gynecological patients with bleeding complications due to various causes. The following case report illustrates another indication for this highly effective but rarely used method.

CASE REPORT

A 41 years old lady with a history of Total Abdominal Hysterectomy with left salpingo–oophorectomy with right salpingectomy done on 18/ 01 /2024 for uterine fibroids. Presented with on and off bleeding per vaginum which started after 1 week and continued for 3 weeks post-surgery. General and systemic examinations were normal. On per speculum examination vault was raw-looking and bleeding was coming through the centre of the vault. All routine blood investigations were within normal limits except drop in hemoglobin level from 11 to 10.5 gm/dl. An ultrasound pelvis was done and ruled out any pelvic collection. After managing with tranexamic acid, and broad-spectrum antibiotics and after proper counseling, the patient was prepared for examination under anaesthesia followed by surgical intervention. Vault was resutured vaginally. She was fine for 3 weeks after surgery when she again started having variable bleeding per vaginum. This time, her Hb was 10gm/dl. CT angiography was done on 13/03/2024 which showed prominent vascular channels in the arterial phase more prominently on the right side which was arising from a branch of the right internal iliac artery. This was suggestive of vascular malformation, and granulation tissue. Figure 1.

After proper counseling, the patient was taken up for Superselective angioembolization of uterovaginal arteries producing a vascular blush on 16.03.2024.

Findings: Right femoral artery access. Bilateral internal iliac arteries were accessed sequentially and anterior division followed by uterine arteries evaluated. Hypervascular blush seen in the region (right >left). (Figure 2a, 2b)

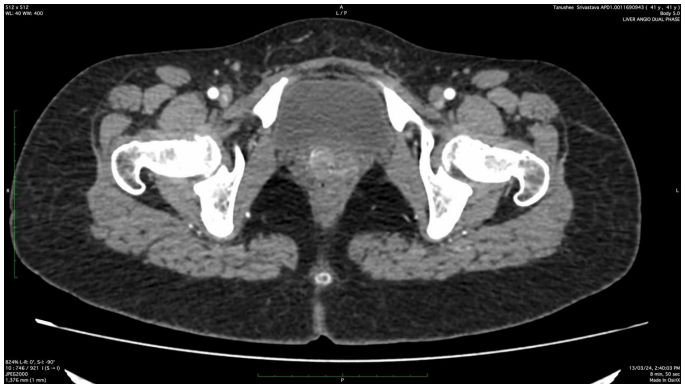

Fig. 1: CT angiography.

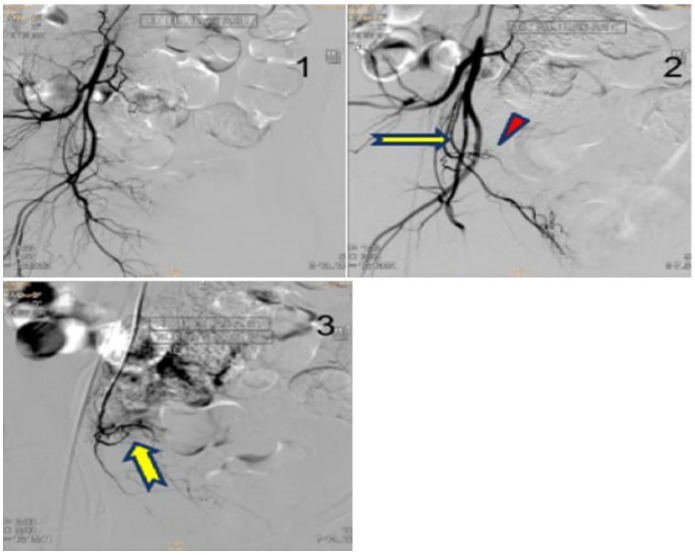

Fig. 2a: Right internal iliac artery

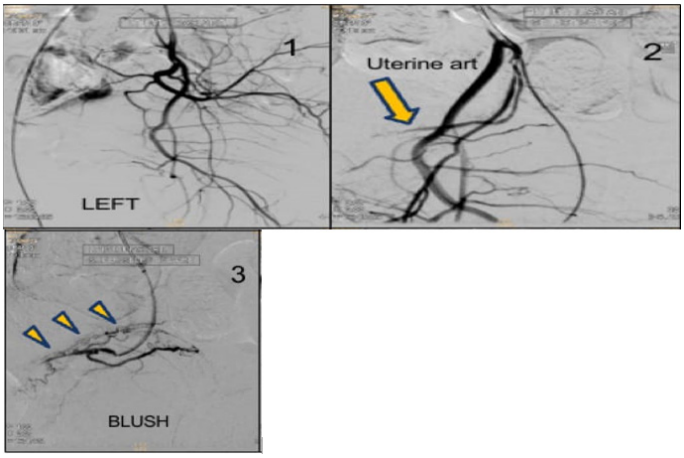

Fig. 2b: Left internal iliac artery

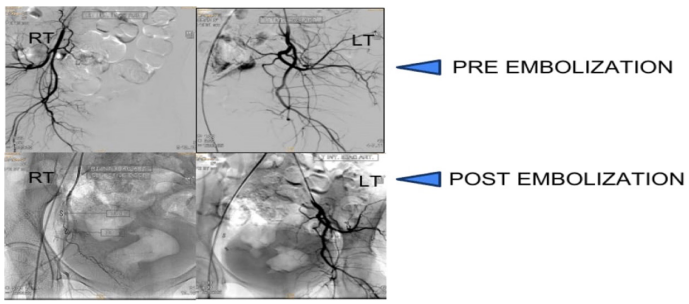

Fig. 3: Bilateral internal iliac artery

PROCEDURE

The patient was laid in the supine position; right femoral incision was given. Super selective angiography is done using a microcatheter in multiple projections. Uterovaginal arteries were identified, engaged, and embolised using gelfoam and fibered coils. Final check angiography shows anterior division of both internal iliac arteries and their branches are patent. Hypervascular blush has been obliterated without any complication (Figure 3). Post-procedure period was uneventful. The patient was kept on broad-spectrum antibiotics and other supportive medications and was discharged on 3rd post-op day (18/03/2024) in stable condition. The patient was followed up on post-op day 13th found to be symptom free. She is doing fine thereafter.

DISCUSSION

Post-hysterectomy vaginal bleeding is not a common problem, particularly in women in whom the cervix has been removed with a reported incidence of 0.2-2 %.[1] It Is common to have on and off blood-stained vaginal discharge for several days to several weeks after hysterectomy as stitches dissolve and tissues heal from resolving granulation tissue. Other causes of post hysterectomy vaginal bleeding include atrophic vaginitis, cervical stump cancer, infiltrating ovarian tumors, bladder pathology, endometriosis of the vault, and vaginal cuff tear secondary to hematoma or infection. The common causes of postoperative bleeding include improperly ligated vessels, dislodgement of clots, hypertension, improper surgical technique, pressure necrosis, subacute infection, and coagulation disorders.[5] Surgical re-exploration was traditionally used to control secondary postoperative haemorrhage. However, it was often associated with surgical complications like infection, bleeding, ureter injury, and the pertinent surgical and anaesthetic risks associated with emergency operations. Hemodynamically unstable patients had relatively more chances of anaesthetic complications. During surgical exploration, bleeding vessels were identified and ligated. Since the pelvis is supplied by extensive anastomosis of blood vessels, the chances of successful control of bleeding were limited if the bleeding sites were extensive or unidentifiable or if there was anatomical inaccessibility of bleeding vessels. Inflammatory reactions including pelvic adhesions are also responsible for the failure of surgical explorations. Pelvic bleeding within the vascular bed resulting from trauma, neoplasms, and surgery can be life-threatening and usually necessitates some type of intervention.[6,7] Blood flow sites within the vascular tree may be reduced by mechanical occlusion of the feeding vessel, such as by embolization. The aim, in most instances, is peripheral occlusion of the vessel to prevent reconstitution by collateral vessels, although the location of the occlusion is dependent on the size and composition of the embolic agent. Ideally, vessel occlusion reduces the blood flow sufficiently to stop the hemorrhage without causing tissue

ischemia or infarction.[7,8,9] Trauma to pelvic arteries may cause life-threatening hemorrhage. The bleeding site can be identified by angiography and trans-catheter embolization is a very effective method of treatment.[5,6] Bleeding from pelvic vascular malformation is very rare. Very few cases have been reported in the literature.

CONCLUSION:

Persistent post hysterectomy Vaginal bleeding is very rare and often misdiagnosed and when other causes have been ruled out, a final diagnosis can be made out by angiography. For recurrent post-hysterectomy vaginal bleeding, vascular malformation should be considered for evaluation. Decisions on surgical/radiological intervention should be taken based on clinical assessment, examination, and proper diagnosis. Hence early recognition, proper diagnosis, and prompt intervention (reoperation or embolization) to arrest bleeding are essential strategies for suitable patient outcomes.

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2. Updating OB-GYNs: Revisiting Genetic Concepts and Latest Technologies for Busy Clinics

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ABSTRACT

Genetics is the central basic science in this century. With decreasing costs and widespread availability of genetic tests, clinicians are taking genetic knowledge from bench to bedside for precise diagnosis and management of patients. Gynaecology and Reproductive medicine are not immune to this revolution.

INTRODUCTION

DNA is at the epicentre of all clinical and laboratory medicine. Reproductive medicine or obstetric clinical practice includes fetal and maternal concerns during preconception, preimplantation, and antenatal period. As genetics becomes a more integral part of routine medical practice, it is essential that obstetrician–gynaecologists be aware of the advances in the understanding of genetic disease and the fundamental principles of genetic screening and molecular testing.[1,2] We describe here 2 cases presented to obstetric clinics where genetic counseling and genetic tests helped in definitive diagnosis and further management.

Each case highlights chromosomal and single gene (monogenic)- two different types of genetic disorders diagnosed by 2 different genetic testing technologies- chromosomal microarray and next-generation sequencing and how genetic counseling helped in a successful pregnancy outcome.

Case 1

A non-consanguineous couple was referred to the genetic clinic by the primary obstetrician due to a history of recurrent pregnancy losses, as indicated in the pedigree (Fig 1). The 26-year-old female had experienced two spontaneous abortions around 6-7 weeks of gestation, both without fetal cardiac activity. Their first pregnancy was terminated at 20 weeks due to multiple fetal malformations detected during an anomaly scan, including spinal abnormalities, hydrocephalus, bilateral clubfoot, and cardiomegaly. Genetic testing was not performed on that fetus. Given the absence of significant family history on either side, the couple sought to understand the cause of their bad obstetric history (BOH) and the risk of similar events recurring. Further evaluation included karyotyping, which revealed

that the wife carried a balanced translocation, 46,XX,t(7;17)(p13; q24). They were informed that there was a 1/3 chance of future pregnancies being affected by an unbalanced translocation.

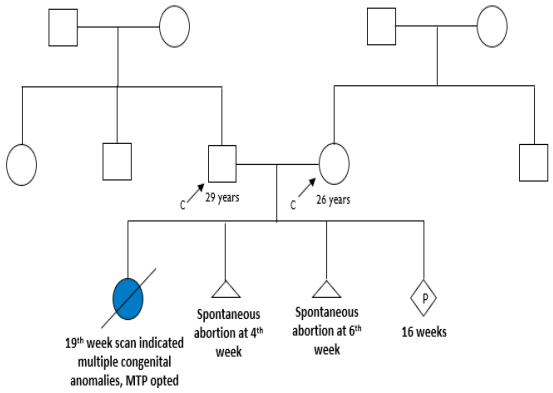

Fig 1: Pedigree showing the detailed family history and previous obstetric history of the couple.

The couple was counseled on alternative reproductive options, such as IVF with Pre-implantation Genetic Testing for Structural Rearrangements (PGT-SR). This procedure allows the selection of embryos without unbalanced translocations for implantation, increasing the likelihood of a successful pregnancy. Following informed consent, the patient underwent IVF and PGT-SR. Four embryos reached the blastocyst stage, and biopsies were taken on day 5 for PGT-SR analysis. Genetic analysis of the blastocysts revealed: Blastocyst 1 had an unbalanced translocation with whole chromosome aneuploidies (46,XA, -7p, +9, -17); Blastocyst 2 had whole chromosome aneuploidies (46,XA, +7, -11); Blastocysts 3 and 4 showed normal euploid chromosomes (46,XA). After discussion with the family, Blastocysts 3 and 4, were selected and implanted. Follow-up revealed successful implantation of one embryo with detectable cardiac activity at 6 weeks of gestation. To further confirm the absence of imbalance as ascertained by the PGT also, amniocentesis was performed at 16 weeks of gestation. The results indicated a normal karyotype (46,XA), confirming a favourable outcome for this pregnancy.

Case 2

A 28-year-old female and 30-year-old male, a non-consanguineous couple married for three years, visited the genetic outpatient department (OPD) to assess the risk of their future children having spinal muscular atrophy (SMA). There was no significant family history of genetic disorders in either partner. During the consultation, the female mentioned a friend's child who tragically passed away at six months from SMA, despite no family history, prompting her to seek thorough precautions for her future pregnancies.

The family was informed that genetic testing could be performed to screen for SMA. They were explained that for autosomal recessive disorders like SMA, both parents must carry a mutated gene and both copies must be passed on to the child for the condition to manifest, with a 25% risk in each pregnancy under these circumstances. After obtaining their informed consent, SMN1 gene analysis and carrier screening for a panel of 1000 genes were ordered for the couple.

Upon reviewing the test results in a subsequent consultation, it was discussed with the family that their risk of having a child with SMA or other screened genetic disorders was low. The husband was found to be a carrier of the SMN1 exon 7&8 deletion, but the wife did not carry the same variant, thus reducing the risk for SMA in their offspring. Similarly, carrier screening identified a few variants in both partners, but no shared variants in the same gene, reassuring the family of a low overall risk for these conditions in their future pregnancies.

DISCUSSION

Case 1

Highlights the utility of chromosomal analysis in couples with bad obstetric outcomes. Chromosomal microarray is a high-resolution technique for diagnosing imbalances in chromosome imbalances (aneuploidies/ copy number variations/ deletions or duplications). Such chromosomal abnormalities are responsible for the majority of the first trimester miscarriages. They are also an important cause of developmental abnormalities like congenital malformations as was seen in the present case. Hence, the chromosomal microarray must be done in a fetus with malformations or in products of conception from an early miscarriage.

Most of the chromosomal abnormalities are sporadic in occurrence. However, there can be repeat imbalance leading to recurrent affection of pregnancies, if one of the partners is a carrier of a balanced chromosomal rearrangement.

In approximately 2%–5% of couples with recurrent miscarriages, one of the partners carries a balanced structural chromosomal anomaly, most commonly a balanced reciprocal translocation. Although carriers of balanced translocation are usually phenotypically normal, their pregnancies are at increased risk of miscarriage and may result in a live birth with multiple congenital malformations and/or intellectual disability secondary to an unbalanced chromosomal arrangement. The risk of miscarriage is influenced by the size and the genetic content of the rearranged chromosomal segments.[3] Balanced rearrangements can be detected only by chromosomal karyotype.

Once a partner is detected to be a carrier of translocation, as was found in the present case- there is a probability of forming unbalanced gametes leading to chromosomal aneuploidies or chromosomal deletions/ duplications in the embryos.

IVF with preimplantation genetic testing of the embryos can be done to detect structurally balanced and unbalanced embryos. Accordingly, embryos can be selected for implantation.

Case 2

Highlights the screening of single gene conditions or monogenic conditions. These are different from chromosomal genetic conditions as they are caused due to mutations or defects in genes and not due to chromosomal imbalances. The monogenic conditions could be further divided according to inheritance in the family into dominant and recessive conditions.

Recessive genetic conditions occur due to one or both partners being carriers of the mutation. They can be screened for at a preconception or prenatal level by testing for carrier mutations in the partners. The test uses next-generation sequencing to detect defects in gene sequences. SMA is a monogenic condition with a carrier incidence of about 1 in 20 in the population.

The ACOG's position on carrier screening is that "ethnic-specific, panethnic, and expanded carrier screening are acceptable strategies for preconception and prenatal carrier screening. Every obstetrician-gynaecologist or other women's health care provider should establish a standard approach that is consistently offered to and discussed with each patient, ideally before pregnancy." [4] No Indian guidelines are available for the same.

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3. Variable Presentation of Tubo Ovarian Abscess

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In the recent past, we have received many tubo ovarian abscess cases out of them two cases are mentioned in this presentation, and each of the cases was unique in presentation. The first case has a larger mass but very minimal clinical features, the second one presented after ovum pickup with fever resistant to antibiotics.

Case 1

Mrs. X, a 32-year-old female came to OPD of Indraprastha Apollo Hospital with complaints of pain in her lower abdomen with low-grade fever. The pain was off and on, especially on the left side with low-grade fever recorded up to 100 degrees Fahrenheit. She was a known case of endometriosis and endometriomas for 8 years. She was already being treated for this fever as had pyuria (Feropenum), and the abdominopelvic mass of 24 weeks in size was dismissed as an endometriotic cyst. The patient had a menstrual history of 5-7/ 30 days with clots with dysmenorrhea and used to take painkillers 2-3 times / day. She has been married since 2016. P1L2 twin baby by caesarean section on 14 Dec 2021, twin babies one male and one female, alive and healthy, IVF conceived pregnancy with donor ovum, history of bladder injury during caesarean section. She was diagnosed with endometriosis 7 years back and had a laparoscopy in 2020 because of infertility and an endometriotic cyst. General examination was unremarkable. On per abdomen mass arising from pelvis ~ 24 weeks size, per speculum – cervix pulled up, purulent discharge coming from os, on per vaginum large mass felt centrally. Investigations and pus culture reports came as E. coli antibiotics according to sensitivity were started.

The patient came with an MRI report of a bilateral large endometriotic cyst reviewed and repeated here at our hospital showed uterine adenomyosis and changes of endometriosis in the pelvic cavity, large endometrioma seen in the Right ovary 6.1X 5.3 cm, large left tubo ovarian cystic lesion 16X11X14 cm was found likely endometrioma with superimposed infection, left-sided ovary not visualized separately. The decision of exploratory laparotomy was taken.

Intraoperative Findings: A large left tubo ovarian cyst was observed approximately 16 X 14 cm in size. Foul smelling, greenish-yellow pus approximately 1500 ml, and sent for culture. Dense adhesion between cyst wall, sigmoid colon, uterus, lateral and anterior pelvic wall. Adhesiolysis done. Right-sided endometriotic cystectomy done and chocolate colored fluid drained. Pus culture showed E.

coli. Appropriate antibiotics according to the sensitivity given. Histopathology: Left ovary: benign hemorrhagic cyst, consistent with endometriotic cyst. Left fallopian tube: severe acute on chronic salpingitis with focal involvement of deep layers by endometriosis. The fever subsided within 24 hours of surgery. The patient fully recovered and went home on day 4 of surgery on tablet dinogest.

Case 2

Mrs. G, a 31-year-old female came to OPD (22.4.2024) of Indraprastha Apollo Hospital with complaints of fever with chills of 12 days duration started 2 days after the day of egg retrieval (8.4.2024). She took multiple antibiotics during this period as advised by her local doctors. Despite this, her fever persisted, reaching 103 degrees, and had persistently raised her TLC count. There was no history of vaginal discharge, weight loss. Typhoid, malaria, and urinary tract infections had been ruled out. The patient had a menstrual history of 5-7/ 30 days, she has been married since 2018, nulligravida. She had a history of Chocolate cyst of the left ovary and infertility. General examination was unremarkable. Per abdomen: 16 weeks vague mass in the lower abdomen. Per speculum – cervix, vulva, vagina healthy. Per vaginum – an abdominopelvic mass -16 weeks. After admission all the relevant investigations were sent and injection of Meropenem was started with other supportive treatments. During treatment Her TLC count and CRP were high. (Procalcitonin-0.50ng/ml, D Dimer-1173ng/ml, FDP-9.87 mcg/ml). Her ultrasound –the left ovary bulky two cystic areas suggestive of dermoid cyst-9.2x7.6x6.8cm and 5x5 cm. MRI -left ovary hemorrhagic cyst left ovary enlarged infected endometrioma with features of peritonitis, given persistently high WBC count and fever Decision for exploratory laparotomy was taken.

Intraoperative Findings: Large cystic mass with thick walled approximately 10 cm size arising from pelvis after opening abdomen –cyst was adherent to the large bowel and to uterus posteriorly and arising from left ovary. The left tube is oedematous and adherent to the cyst. The uterus right tube and ovary appeared normal. After extensive adhesiolysis left salpingo-oophorectomy was done under general anesthesia and the specimen was sent for histopathology and it showed left ovary–marked acute on chronic oophoritis with prominent areas of suppurative necrosis and abscess formation. Left fallopian tube – moderate acute on chronic salpingitis. All cultures (pus, blood) negative. Then fever subsided within 24 hours of surgery. The patient fully recovered and went home on day 4 of surgery.

DISCUSSION

Tubo-ovarian abscess, (TOA), is a serious sequela of pelvic inflammatory disease. TOA has been reported to occur in as many as 34% of patients who were initially diagnosed with PID.[1] TOA, similar to PID, occurs usually in women of ages 20 to 40. Up to 59% of these women are nulliparous.[2] The organisms obtained from polymicrobial TOAs are a mixture of anaerobic, aerobic, and facultative organisms. The most frequently isolated organisms include Escherichia coli (37%), Bacteroides fragilis (22%), and other Bacteroides species (26%).[3] On examination, patients with PID may exhibit muscular guarding, cervical motion tenderness, and occasional rebound tenderness. There is usually purulent cervical discharge visualized. Adnexa are frequently moderate to severely tender, with palpable mass or fullness.[4] Imaging techniques available to diagnose TOA are ultrasonography, radionucleotide scans, computed tomography (CT), and laparoscopy. Among these options, laparoscopy is considered the gold standard for diagnosis of TOA.[5] Prompt diagnosis of a TOA is imperative to avoid sequelae of TOA rupture and may give the patient the best opportunity to respond to antibiotics. Current research has also shown the use of broad-spectrum antibiotics is successful in treating patients with TOA.[6-13] Successful management of TOA requires an accurate and timely diagnosis. It has been reported that up to 35% of patients who were admitted with PID had a tubo-ovarian abscess.[14] This misdiagnosis may explain some of the failures that occur with the management of PID, and possibly be a major factor for infertility in patients diagnosed with PID. TOA causes more than 80% of the failures of PID management.[15] Surgical intervention appears to be appropriate in patients who present with acute surgical abdomen and ruptured TOA is suspected, when a patient who is being treated with intravenous antibiotics and not responding increase in WBC count, increase in size of TOA, worsening abdominal pelvic pain, patients with abscesses and who have completed childbearing, and the postmenopausal patient. The exact timing of the surgery may be difficult and should be based on clinical findings and patient desires.[16]

CONCLUSION:

A tubo-ovarian abscess (TOA) is a complex infectious mass of the adnexa that forms a sequela of pelvic inflammatory disease. Classically, a TOA manifests with an adnexal mass, fever, elevated white blood cell count, lower abdominal-pelvic pain, and/or vaginal discharge; however, presentations of this disease can be highly variable. The management of TOA has evolved since the early twentieth century. In cases of ruptured TOA, immediate surgery is now the standard of care and, if fertility is desired, data suggest conservative options may have favorable outcomes. Current options for unruptured cases include treatment with antibiotics alone, laparotomy after medical management failure, or emergent laparoscopy with medical management and interventional radiology. Surgical options for non-responders to medical management are mostly TAH/BSO, and less frequently, laparoscopic drainage and irrigation. Conservative laparotomies include posterior colpotomy among others.

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Journal Scan

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A follicular volume of >0.56 cm3 at trigger is the cutoff to predict oocyte maturity: a starting point for novel volume-based triggering criteria

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Fertil Steril. 2024 Jun;121(6):991-999

AIM

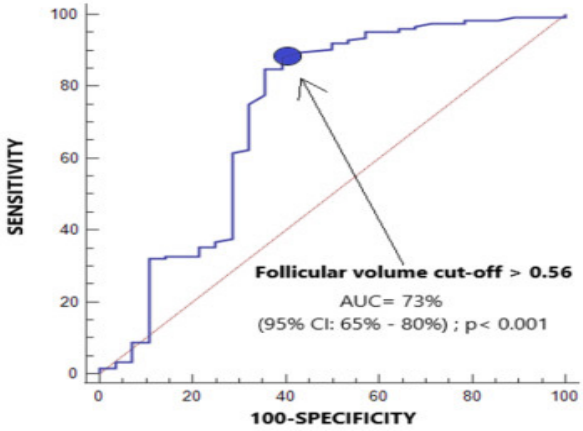
To determine the trigger day follicular volume that will correspond to a mature oocyte at egg retrieval and to calculate the mean follicular growth using SonoAVC follicle.

MATERIAL AND METHODS

Women in whom it was possible to identify follicles using ultrasound (SonoAVC follicle) both on the day of trigger and on the day of egg retrieval were recruited. Follicles that had the desired volume were selected. Follicular growth was defined as the difference in follicular volume between the ultrasound performed on the day of the trigger and the ultrasound performed in the operating room just before egg retrieval. The primary outcome was the relationship between follicular volume on the day of the trigger and the oocyte maturity stage. The secondary outcome was the follicular growth rate from the day of trigger to the day of oocyte retrieval, as measured using SonoAVC follicle.

RESULTS

Among the final 206 follicles on trigger day from 53 women follicular volume to oocyte maturity relationship was studied in 153 follicles. An area under the curve value of 0.73 (95% CI: 0.65–0.80, P<.001) was obtained in the type II ROC curve generated, after confirmation of follicular content by individualized puncture. A sensitivity of 85% and a specificity of 64% for predicting oocyte maturity was obtained for a follicular volume of >0.56 cm3, the cutoff point with the highest Youden index as shown in Figure 1 below. This meant a 73% probability that the model would distinguish between a follicle that will contain a mature oocyte and one that will not. Also, a positive relationship was observed between follicular volume on the day of ovulation induction and its growth (r = 0.33, p <.001). Another observation was spontaneous rupture in follicles of >2 cm3 with an even increased risk in bigger follicles of size >3 cm3.



Follicular volume	>0.56 cm³
Sensitivity	85% (77%-91%)
Specificity	64% (44%-81%)
Positive likelihood ratio	2.4 (1.44-3.92)
Negative likelihood ratio	0.2 (0.14-0.39)
Positive predictive value	91% (87%-95%)
Negative predictive value	49% (37%-61%)

Fig. 1: Type II receiver operating characteristic curve for sonography-based automated volume count (SonoAVC) as a tool to predict oocyte maturity and the cutoff point with higher sensitivity and specificity. AUC = area under the curve; CI = confidence interval

CONCLUSION

Sonography-based automated volume count (SonoAVC) is found to be accurate to in predicting follicular volume. In this study, they found oocyte maturity to be related to follicular volume on the day of trigger rather than the day of oocyte retrieval. They concluded a greater probability of obtaining a mature oocyte from follicles with a volume of >0.56 cm3 on the day of trigger. Thus follicular volume measured using 3D-US is a useful parameter in assessing oocyte maturity.

Comparison of the Efficiency of Magnetic-Activated Cell Sorting (MACS) and Physiological Intracytoplasmic Sperm Injection (PICSI) for Sperm Selection in Cases with Unexplained Infertility

Ahmadi A, Sobhani A, Khalili MA, Agha-Rahimi A, Nabi A, Findikli N
J Reprod Infertil. 2022 Jul-Sep;23(3):184-191

BACKGROUND

Couples with unexplained infertility may have an abnormality in their sperm in the form of DNA fragmentation. Advanced sperm selection techniques such as MACS (de-selects the apoptotic sperms) and PICSI (selects HA-bound sperms) can be used to separate sperm with intact DNA, especially in men with teratozoospermia. The purpose of this study was evaluating the efficacy of MACS and PICSI techniques in selecting sperms with the lowest DFI(DNA fragmentation index) rates.

MATERIAL AND METHODS

A total of 20 semen samples were collected from couples with unexplained infertility and prepared with the swim-up method after completing semen analysis according to WHO. Sperm DNA fragmentation rates were calculated for various methods – semen only, swim-up, motile sperms after swim-up, MACS sperms, and PICSI sperms. MACS sperms were examined by MSOME (Motile sperm organelle morphology examination). Statistical analysis was done using GraphPad Prism ($p<0.05$ statistically significant).

RESULTS

DFI values in both PICSI and MACS groups were significantly reduced as compared to the swim-up group. Reduction rates of swim-up, swim-up selection, PICSI, and MACS groups were 28.9±14.93, 36.66±12.50, 58.04±9.76, and 70.70±10.39, respectively. There was a significant correlation between DFI of the PICSI group with the DFI swim-up suspension ($p=0.01$ and $r=0.59$, CI: 0.13-0.84). There was a significant correlation between the DFI of the MACS group with the DFI of swim-up suspension ($p<0.001$ and $r=0.74$, CI: 0.44-0.89). Using processed sperms after swim-up, PICSI, and MACS were found to provide an additional DFI reduction of 36.57±15.52 and 58.20± 13.02, respectively. Also, it was observed that MACS sperms had low motility but normal morphology.

CONCLUSION

As we know, sperm DNA fragmentation has a possible negative impact on implantation and live birth rates. So sperm selection by advanced techniques will allow choosing the most appropriate sperms for the setting of ICSI. Although the study data showed that both PICSI and MACS could not completely eliminate the sperm with fragmented DNA, MACS had a higher potential for DFI reduction rate compared to PICSI. It was also concluded that the MACS method can improve DFI but without improving the sperm parameters and quality.

A comparative evaluation of sub-endometrial and intrauterine platelet-rich plasma treatment for women with recurrent implantation failure

Noushin MA, Ashraf M, Thunga C, Singh S, Singh S, Basheer R, Ashraf R, Jayaprakasan K
F&S Science. 2021 Aug 1;2(3):295-302

BACKGROUND

Recurrent implantation failure (RIF) is the failure to achieve a clinical pregnancy after the transfer of at least four good-quality embryos in a minimum of three fresh or frozen cycles in a woman aged <40 years. One of the causes of RIF is poor endometrial receptivity. Platelet-rich plasma (PRP), a concentrate of autologous PRP protein derived from whole blood, has been tried by several clinicians in patients with refractory thin endometrium. The principle behind its use is the release of implantation-friendly growth factors and cytokines which increase endometrial proliferation and vascularity by concentrating the platelets up to 94% by a reversal of platelet to RBC ratio. Being derived from one's own blood, PRP is safe and free from viral infections and immunologic reactions. A comparison of the administration of activated PRP into the sub-endometrial space of the uterine cavity (SE-PRP) rather than infusing it into the endometrial surface (intrauterine; IU-PRP) was the purpose of the study. Intrauterine infusion has a risk of lower than desired quantity at the action site as part of it may be flushed off, the sub-endometrial route on the other hand, being the niche site of growth factor synthesis and regeneration may be better.

MATERIAL AND METHODS

A prospective observational cohort study was undertaken in a tertiary fertility unit where women aged <40 years with a history of recurrent implantation failure underwent frozen embryo transfer (FET). In SE-PRP, PRP was injected into the sub-endometrial space transvaginally in the luteal phase of the previous cycle of embryo transfer under ultrasound guidance (n= 55). SE-PRP was administered under conscious sedation as a day-care procedure. In IU-PRP, PRP was injected in the current FET cycle when the endometrial thickness was approximately 7 mm (n=109). The control group consisted of women who did not choose PRP treatment and underwent standard FET with no intervention (n=154). Statistical analysis was performed using SPSS (version 20)(p-value < 0.05 taken statistically significant). Logistic regression analysis was performed to evaluate the effect of variables on LBR/OPR.

RESULTS

Ongoing pregnancy rate(OPR) (defined as pregnancy continuing beyond 20 weeks) per transfer cycle and live birth rate (LBR) (defined as live birth of an infant after 24 weeks) per transfer cycle were estimated. OPR/LBR was higher in the SE-PRP (22/55,40%) and IU-PRP(45/109,41.3%) groups compared to the control group (34/154, 22.1%). Similarly, clinical pregnancy rate CPR was higher in the SE-PRP (28/55, 51%) and IU-PRP (57/109, 52.3%) groups compared to the control group (52/154, 33.8%). No statistical difference in the LBR/CPR was noted between the SE-PRP and IU-PRP groups. The miscarriage rate was similar in all three groups (14/55, 25.45%; 25/109, 22.23%; and 34/154, 22.07%, respectively). In both univariate and multivariate analysis, PRP treatment was the significant variable influencing the outcomes favourably. None of the patients in either study group developed any adverse reaction or infection or bleeding during or after the procedure.

CONCLUSION

In women with a history of recurrent implantation failure, PRP treatment appears to improve FET outcome in the form of an increase in OPR/LBR. However, study data showed no benefit of using the invasive sub-endometrial route over lesser invasive IU-PRP treatment. Further, a larger scale RCT design study is warranted to generate high-quality evidence on its regular use in cases of RIF.

News Flash

Dr. Jaya Chawla

Professor

Department of Obstetrics and Gynaecology, ABVIMS & Dr RMLH

Thanks to a global world, Roe and Wade seem to have become household names in all nooks and corners of the world. Roe a pseudonym for a woman who was both unmarried and unemployed filed a suit against a law that denied women abortion rights in the state of Texas, claiming that her fundamental right to privacy, which included reproductive rights granted by U.S.Federal Laws, had been violated. Wade was the Attorney against whom her plea was. All the years that the case took to get decided witnessed Roe begetting the child but the decision held up Roe's plea that women were entitled to reproductive rights including a right to willfully terminate a child not desired.

All the hue and cry that we witness on the streets of Texas, Indiana, Florida and almost the entire United States today are a result of this landmark decision in the history of the US being overturned in a fresh turn of events. It would seem obvious that the women will take to the streets to demand the restoration of their fundamental right to procreate or not to do so. What is stranger is that as per Times of India News on June 17th, anti-abortion groups are hogging the actual and virtual space by their attempts to alter the discourse in their favour. The examples are endless. They resort to initiatives that incline people to remove their signatures from pro-abortion petitions, introduce competing ballots that are aimed at confusing the voters, and cause unwarranted delays in the process by resorting to lawsuits over the language of pro-abortion bills.

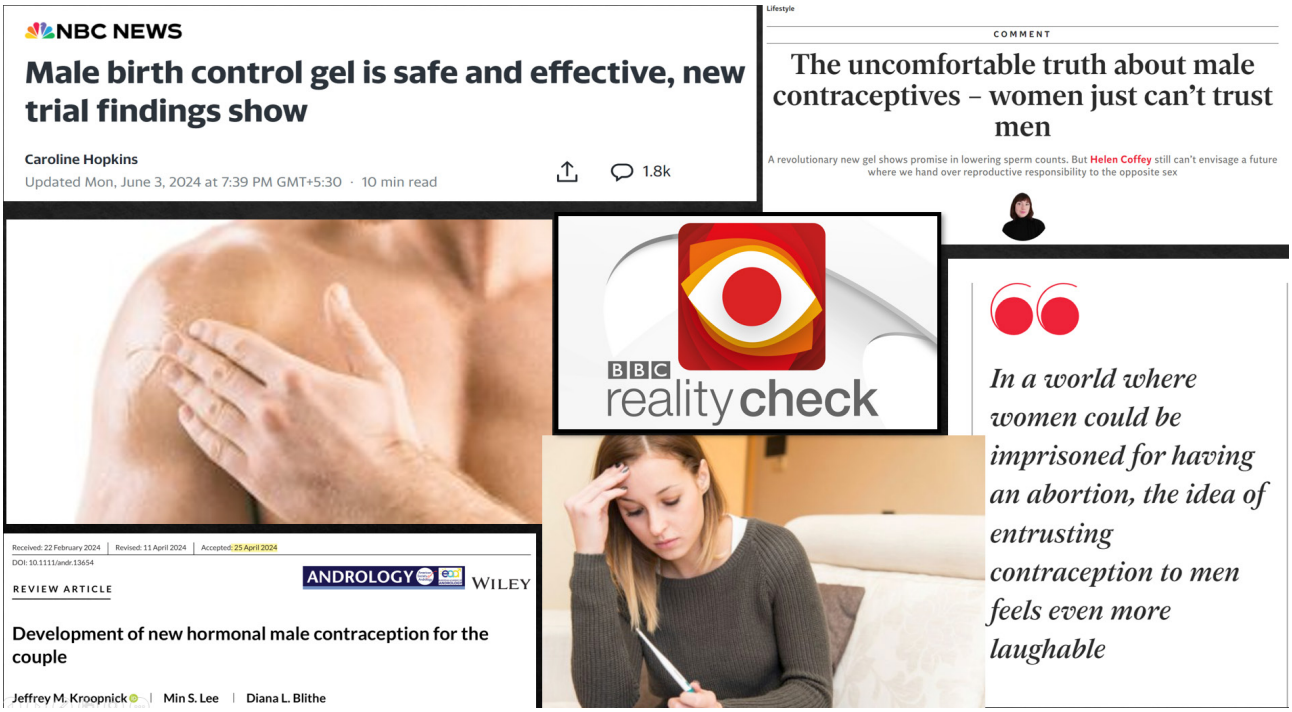
Despite having witnessed their strategies thwarted in Ohio last year, they continue to reinforce the same in other parts of the US, including South Dakota where the lawmakers have passed a bill that enables people to retract their signatures from past petitions. This is followed by numerous concerted efforts to convince people to retract their past endorsements.

These differences originate in part from the dichotomy in US court rulings themselves. While the right to abortion was curtailed to a great extent by the overturning of the verdict in the Roe Vs Wade case two years ago, the US Supreme Court recently issued a ruling that upholds the use of the abortion pill, Mifepristone. The implications of these decisions on the masses are going to be widespread and far reaching. It could either make youngsters more responsible

in their contraceptive practices or make monogamy more popular. On the other hand, those in doldrums about whether to continue pregnancy would rather quickly terminate than take a moment to ponder over their decision lest they lose the right to terminate, altogether.

Boon or bane remains to be seen. After all, you have to live through the storm to be able to see where you land with it, the altar or the pedestal.

Male contraceptive gel: A boon until proved otherwise!



Contraception has primarily been a women-centered domain, thus far, partly because of the lack of many appealing options for the male counterpart. High failure rates of barriers and the irreversibility of vasectomy have deterred many caring husbands from shouldering the responsibility they would so much love to. If NBC News dated June 3 2024, is to be believed, then that scenario is about to witness a sea change.

The phase 2 trials of a gel (Blithe and Myer 2023) that needs to be applied as a teaspoon full daily, to both shoulder blades, much akin to a sanitizer in fragrance and consistency, are close to completion. The gel which consists of testosterone and progesterone, after consistent use of 8 weeks is reported to lower sperm count to the desired threshold of less than a million per milliliter. The hormonal levels are consistent as measured in serum and levels are such that no diminution of libido is reported. The median time to revert back to a count of > 20 million/ ml is a little over 3 months.

With these promising results there is a user-controlled, non coitus dependent, systemically administered male contraceptive without the need for invasive injectables/ implants and also obviating frequent visits to the medic. However, that would be too rosy a picture in isolation.

In a world where stealthing is not just new lingo, but a new way of life for some, where a certain species is fully entitled to disappear into thin air should *something* happen, where women would be denied the right to abortion in the garb of protecting the rights of the hitherto unborn, the question that looms large is, how many women would find it safe to entrust themselves and their reproductive responsibilities to the proverbial *shoulder blades* of their counterparts. Until we have hardcore answers, let's take the privilege of believing, that the gel shall absolve many women of an as yet solitary pursuit.

Snitch Snatchers

Dr. Preeti Sainia
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1. Which Type of Male Infertility Is Most Common
   A. Testicular B. Pretesticular
   C. Post testicular D. idiopathic
2. All is True About Sawyer Syndrome Except
   A. 46 XX
   B. Named by Gerald Sawyer
   C. Have typical female external genetalia
   D. Can become pregnant by IVF and donor oocyte
3. Men With Diabetes Typically Have
   A. Low sperm count
   B. Increased sperm DNA fragmentation
   C. Higher degree of oxidative stress
   D. All of the above
4. The stage of meiosis in which the oogonia are arrested at birth is
   A. anaphase B. metaphase
   C. prophase I D. telophase I
5. Following syndrome is marked by hypothalamic amenorrhoea
   A. Kallmann's syndrome
   B. Polycystic ovarian syndrome
   C. Noonan syndrome
   D. Ashermans syndrome
6. Ultrasound parameters predicting higher pregnancy rates are all except
   A. tripple layer endometrium 8 to 12mm
   B. ovarian stromal artery PSV>10 cm /sec
   C. uterine artery PI > 3
   D. Endometrial power doppler area >5 mm2
7. The mean follicular growth rate in a stimulated cycle is
   A. 2mm/day B. 1.2 mm/day
   C. 1.7 mm/day D. 1mm/day
8. Commonest chromosomal anomaly associated with infertility in males is
   A. Klinefelter's syndrome
   B. Y chromosome microdeletion
   C. Robertsonian Translocations
   D. Chromosome Inversions
9. Which of the following is the new approach to improve implantation rates in IVF cycles
   A. Endometrial scratching
   B. intrauterine insemination
   C. hysteroscopy
   D. laproscopic surgery
10. What is the recommended first line treatment for couples with unexplained infertility
    A. IVF
    B. ICSI
    C. expectant management
    D. IUI with ovarian stimulation

Answer Key to Quiz 2, July 2024

1. Zolikofer
2. Monopolar surgical instrument
3. 6 cm
4. Infection
5. 10 mm
6. All of the above
7. Elevation angle
8. Dissecting
9. Left upper quadrant insertion
10. Extraction

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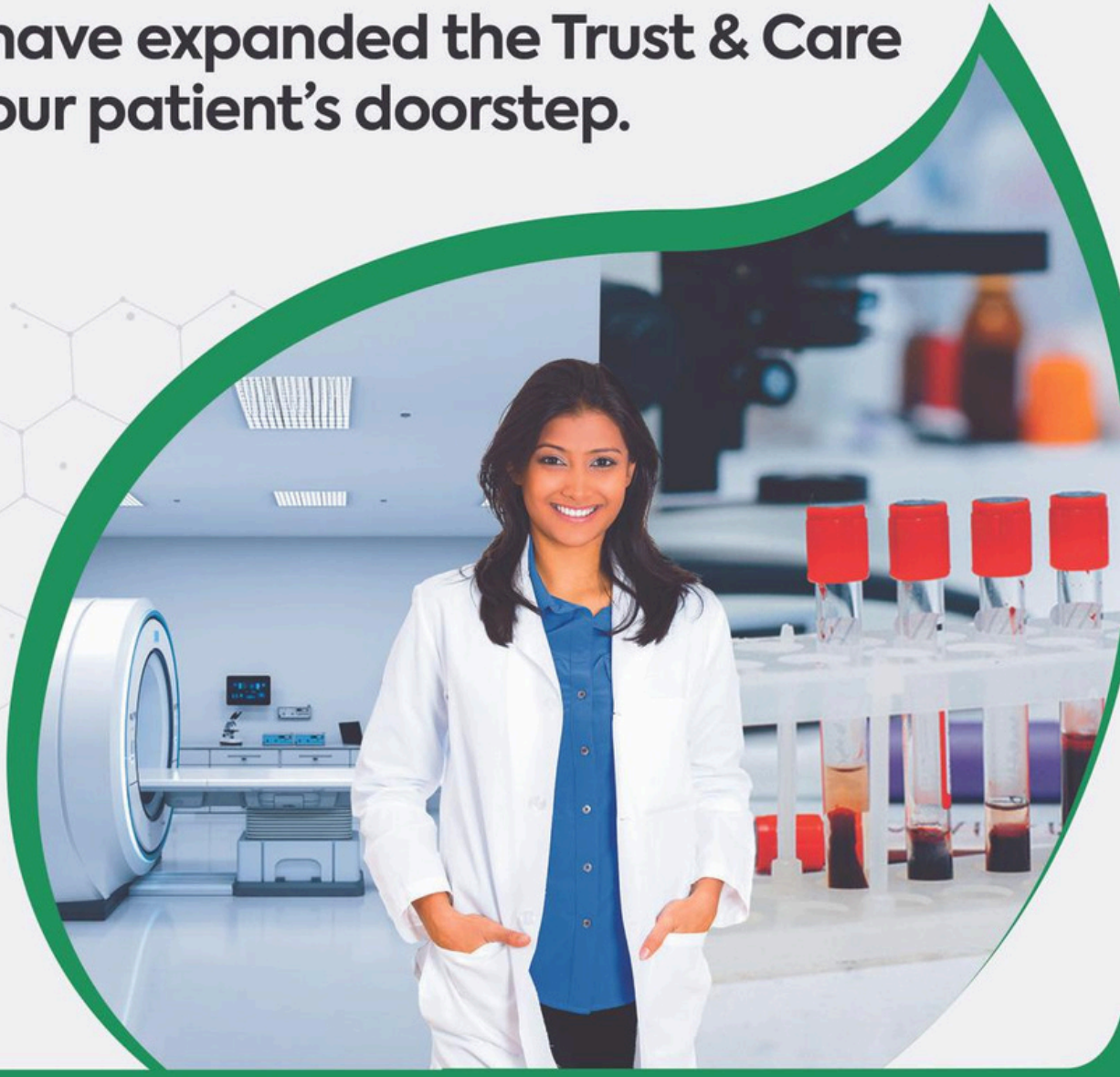

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