

NARCHI BULLETIN

Sir Ganga Ram Hospital, New Delhi, 2024-25

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THEME: "REPRODUCTIVE MEDICINE & ENDOCRINOLOGY"



UPDATE KNOWLEDGE UPGRADE SKILLS UPLIFT WOMEN'S HEALTH



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Infertility is a disease that afflicts one in seven couples in the reproductive age group. Female age is the biggest determinant of fertility. The age at first childbirth has steadily risen over the past decades with the median age at first child-birth reaching more than 30 years in the Global North and 23 years in low and middle income countries like India. This augurs poorly for spontaneous conceptions especially for those women who fall at the low end of the ovarian reserve spectrum.

Assisted reproductive technology is often used to overcome the barrier of infertility. About one in twenty babies born in Australia and one in 500 babies born in India is IVF conceived.

This issue of NARCHI Delhi Bulletin, aims to understand the language of infertility and ART, to help both the Generalists and the Specialists investigate, interpret, treat and counsel women who are sub-fertile or those conceiving through IVF.

Signing off here, with thanks to our contributors : Dr. Sabina, Dr. Megha Solanki & Dr. Hemant Himanshu Parihar; Dr. Tejashri Shrotri; Dr. Swati Shivhare; Dr. Neeti Tiwari & Dr. Nitisha Verma; Dr. Tanu Sharma; Dr. Kashika Kathuria & Dr. Sonal Gupta.

Sincerely,
The editorial team
Mamta Dagar, Ruma Satwik, Sakshi Nayar

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Warm Greeting to Everyone !

It is our great privilege and pleasure to write a message for this bulletin. We had concluded a highly successful and satisfying 31st Annual Conference of NARCHI Delhi Chapter at India Habitate Centre from 8th August to 10th August 2025. We managed to organise pre conference and post conference focussed and dedicated workshops. All institutions from all over Delhi participated in these workshops. In the main conference we had participation of faculty from all over India. The orations were delivered by eminent personalities like Dr. S. Shantha Kumari, Past president of FOGSI and Dr. Bhaskar Pal President Elect of FOGSI. The delegates from all over Delhi as well as NCR participated with great enthusiasm and vigor. We had 1200 registration for the workshops and approx. 300 registration for the main conference.

This bulletin has a Theme of "Reproductive Medicine & Endocrinology". Eminent Senior faculty members have contributed scientifically for this bulletin. This edition deals with topics like "When NOT To Refer for ART?", The ART conceived pregnancy is special, so "What Should You Know about a Referred ART Conceived Women?", The Intrauterine Insemination remains a modality to help patients conceive "TRICKY Situations in Ovarian Stimulation for Intrauterine Insemination was written. There are issues of Genetic problems in recurrent pregnancy loss, the topic of "Should Preimplantation Genetic Testing Be Offered to Women With Recurrent Pregnancy Loss ?" remains relevant for this specific group. These are quite a few cancer survivors who desire to have a family. "Fertility Preservation in Cancer Patients. Managing Expectations with Reality", Adolescents are our future "Management of Androgen Excess in The Adolescent" has been nicely written and their problems discussed. Newer drugs are being developed for the better clinical outcomes. The article "Oral GnRH Antagonist: The New Kid On the Block. What You Can & Cannot Do With It" is very relevant. Managing the Male infertility is an integral part of managing our couples. "Interpreting Abnormal Semen Analysis & The Next Steps", has been optimally written to address this problem.

This bulletin gives a complete bouquets of topics on reproductive medicine. We are sure that our readers will highly benefit from these scientific articles.

Festive season is here, wishing all the NARCHI members happy Navratri as well as Prosperous Diwali. Enjoy reading the bulletin while enjoying the festivals, keep updated, keep upgraded.

Long Live NARCHI Delhi Chapter !!

When NOT to Refer for ART



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Certainly there are certain medical conditions where assisted reproduction is a contraindication and clearly one should not refer the patients. In this article we will discuss when should we not refer a patient to assisted reproduction prematurely when less invasive and cost effective strategies are available.

Infertility is a condition defined by the inability to conceive after one year of unprotected intercourse (or six months for women over 35). While assisted reproduction is a highly effective and well-known treatment. Certainly it should not be a default option. A premature referral to in vitro fertilisation (IVF) not only puts financial burden, but also an emotional and physical challenge for the patient.

A patient-centred approach to infertility care should be done that involves a stepped-care model, starting with a comprehensive diagnostic workup followed by the least invasive and most appropriate treatment for the identified cause. A thorough medical evaluation and investigations should be considered to decide when to refer a patient for assisted reproduction. Here we discuss some of these clinical scenarios where early referral to assisted reproduction is not always indicated.

Ovulatory Dysfunction. Most common example of this condition is Polycystic Ovary Syndrome (PCOS). The primary issue with PCOS is not that these women are infertile but it is anovulation where ovaries do not release egg every menstrual cycle due to hormonal imbalance. This is the main culprit preventing these patients to get pregnant. Directly referring these patients to IVF will not be ideal in these cases. Ovulation induction which aims to stimulate the ovaries so that ovulation can happen is the initial treatment. This is generally achieved with oral medications like Clomiphene Citrate and Letrozole. Directly referring the patient to assisted reproduction, bypass the basic and simple approach for underlying cause adding stress to the patients. Most of these patients respond to these oral medications. The ovulation can be documented through ultrasound or serum progesterone. Assisted Reproduction should be reserved in case of clomiphene failure or if associated factors like male factor or tubal issues present, making the simple treatment unlikely to succeed.¹ A majority of anovulatory PCOS patients will respond to these simple medications. IVF is not the only solution for PCOS-related infertility. Ovulation induction should always be the first approach so that we can give a fair chance to patients before proceeding with assisted reproduction.²

Tubal factor

One of the leading causes to infertility is the tubal factor. While bilateral tubal block seen on Hysterosalpingogram (HSG), is considered a direct indication of assisted reproduction, but it is not always the case. Spasm of utero tubal junction muscles during HSG is quite common, giving a false positive result for a block.³ This many a times leads to direct referral to assisted reproduction. This

can be rechecked and a stepwise approach is to be taken. The options include repeat HSG using some muscle relaxants and anti spasmodic which can help relaxing the muscles or a different type of catheter can be used during HSG procedure. Many a times we can see tubes are open after taking these precautions making it false positive report. Other options include sonosalpingogram but the most accurate is laparoscopy with chromopertubation to see the tubal status. This can be combined with hysteroscopic tubal cannulation before stepping directly to assisted reproduction. Once corrected, patient may be able to achieve natural pregnancy if all other factors are within the normal range.

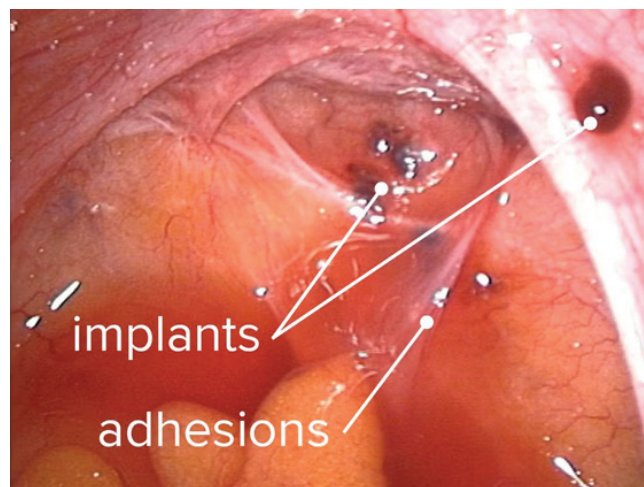
Unexplained Infertility

The diagnosis of unexplained infertility is often very stressful. Despite all normal tests, sometimes it become very difficult to counsel the patient what actually preventing her to get pregnant. Although it doesn't always indicate that we automatically refer the patient directly for advanced technologies. A stepwise approach is also the mainstay here. Factors like female age, duration of infertility and ovarian reserve tests (Serum anti- mullerian hormone and antral follicle count) have to be considered to decide targeted treatment for the patient.

Ovulation Induction with IUI: A few cycles of ovulation induction with oral medications (like clomiphene citrate or letrozole) and/or gonadotrophins combined with Intrauterine Insemination (IUI)⁴ can be considered as initial treatment for these patients. This procedure significantly less invasive and cost effectiveness.

The Role of Diagnostic Laparoscopy

Although unexplained infertility means that standard tests have not revealed a cause. If several cycles of IUI are unsuccessful, or based on patient's symptoms (e.g., pelvic pain, dysmenorrhoea), a diagnostic laparoscopy can be considered before moving on to IVF. Laparoscopy can be planned in these conditions to detect certain conditions like endometriotic spots, pelvic adhesions involving tubes and ovaries which are preventing the natural pregnancy and may not be visible on imaging tests like ultrasound or hysterosalpingogram. Apart from diagnosis, laparoscopy has therapeutic role also that makes it a valuable tool. Couples who are eager to find a definitive answer of infertility before pursuing more complex treatments can be offered laparoscopy.



Picture 1- Endometriosis spots and pelvic adhesions diagnosed on laparoscopy

When IVF is indicated in unexplained infertility.

Patients with advanced maternal age, long duration of infertility or associated infertility factors like abnormal semen parameters or tubal factor can be counselled about the prognosis and decision can be taken accordingly

Young couples with short duration of infertility

Premature rush for assisted reproduction is often seen due to stress and family pressure in young couples. Thus, pushes them to seek a quick fix treatment. Reassurance, counselling and timed intercourse during fertile period is generally suggested before referring patient to infertility work up. Initial assessment and work up of both the partners including semen analysis for male and hormonal evaluation of female partner should be included.

Mild Male Factor Infertility

Mild male factor infertility is a scenario where a semen analysis shows a slight abnormality in sperm count, motility, or morphology, but the values are not low enough to warrant immediate IVF with Intracytoplasmic Sperm Injection (ICSI). Firstly simple lifestyle modifications can be tried and can have a positive impact on sperm parameters.⁴

Cessation of smoking and limit alcohol- Both smoking and alcohol negatively affects the semen parameters

Weight management- encouraging a healthy diet and exercise improves sperm parameters including sperm count and motility.

Role of anti-oxidants- Supplementation with

vitamin c, vitamin E and CO Q 10 have shown to improve overall sperm parameters. Although more evidence is required.⁵

Role of clomiphene and letrozole- this is mainly beneficial in case of hormonal imbalance and obesity. Due to excess adipose tissue in obese men, there is conversion of testosterone to estrogen under the action of enzyme aromatase. This results in low testosterone estrogen ratio leading to hypogonadism.⁶

Stress management- Stress interferes with male hormones and affect sperm parameters.

Intrauterine insemination (IUI)- IUI with ovulation induction can be given as initial approach with mild male infertility. IUI cycles can be attempted in these cases before proceeding with more complex assisted reproduction.⁷

Endometriosis

Endometriosis is a condition where tissue similar to the lining of the uterus grows outside of it, which can cause pain and infertility. The severity of the endometriosis plays a crucial role in deciding the treatment plan.

For mild to moderate endometriosis without significant tubal damage, surgical treatment to remove the endometrial implants may improve fertility. Following surgery, couples can try to conceive naturally or with IUI. Only in cases of severe endometriosis that has caused significant anatomical distortion or tubal damage, or when prior treatments have failed, should IVF be considered as a primary treatment.⁸

Endometriosis Stage 1-II

Less invasive strategies can be applied while minimising the cost and emotional stress to the patient. All the factors including tubal patency, patient clinical history and male factor has to be evaluated.

Couples with stage 1-II endometriosis, ovulation induction with IUI can be considered as initial treatment. OI-IUI improves cycle fecundity versus expectant management and is less invasive/costly than IVF. After 3–6 failed OI-IUI cycles, long infertility duration, significant male factor, bilateral tubal disease, or if patient preference prioritises time-to-pregnancy. IVF is effective but not mandated up-front in Stage I-II disease.⁹ Indications of IVF includes failed IUI, advanced disease, associated male or tubal factor, or long duration of infertility.¹⁰

A detailed evaluation for both male and female partner is required. A step wise approach including history, examination and investigations have to be taken into account before deciding treatment.

While IVF has revolutionized reproductive medicine and offers hope to many, it is not a one-size-fits-all solution. By understanding the causes of infertility and exploring less invasive and more affordable options like ovulation induction and IUI or even just explaining the importance of fertile period in selected couples, one can increase their chances of success while minimizing the physical, emotional, and financial strain. Root cause has to be targeted and individualised treatment has to be planned.

One of the most significant reasons for a cautious, tiered approach to infertility treatment is the substantial psychological and financial burden of IVF. Research consistently shows that the stress of the process, which involves daily injections, frequent monitoring appointments, and the emotional rollercoaster of a potential failure, is a leading reason for couples discontinuing treatment. The cost of a single IVF cycle can be prohibitive, often exceeding the cost of several IUI cycles. Therefore, a staged approach protects patients from unnecessary stress and financial strain.

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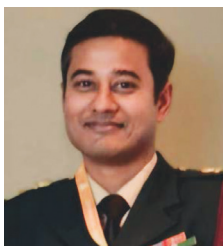
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"What Should You Know About a Referred ART conceived woman"



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Since the inception of assisted reproductive technology (ART) in 1978, it has transformed the management of subfertility and has become a beacon of hope for countless couples in achieving their dream of parenthood. With rising success rates and broader accessibility of ART, there is a growing cohort of pregnancies conceived via ART that are subsequently referred to general obstetrics care for antenatal follow-up and delivery planning.

A referred ART- conceived woman often presents with unique clinical, emotional and psychological considerations, that differ from those of naturally conceived pregnancies. Understanding her ART journey and potential risk factors is essential for optimizing maternal and fetal outcomes.

In this article, we have tried to navigate the challenges specific to such pregnancies and the best management at every step. To ensure a seamless transition of care and provide essential information for the optimal management of this pregnancy conceived via ART, we have tried to summarize the crucial information in the form of a referral checklist, which is enclosed at the end.

Pathophysiology

ART pregnancies are associated with a heightened incidence of obstetric complications, partly attributable to the underlying infertility diagnoses, multiple embryo transfers, and ART procedures themselves. The manipulation of gametes and embryos, as well as the potential epigenetic influences of in vitro culture, may contribute to altered placental development and fetal growth trajectories.

Obstetric Risks Specific to ART Pregnancies

a. Multiple Pregnancies- Incidence is estimated at 20-30% in ART, significantly higher than spontaneous pregnancies (~1%). Risks associated with multiple pregnancies include preterm birth (<37 weeks), low birth weight, neonatal morbidity, maternal hypertensive disorders, and increased cesarean section rates. The European Society of Human

Reproduction and Embryology (ESHRE) recommends elective single embryo transfer (eSET) wherever feasible to reduce multiple gestations¹.

- b. Preterm Birth & Intrauterine Growth Retardation (IUGR):** driven by uteroplacental insufficiency, especially in multiple pregnancies, or placental abnormalities. Antenatal care requires serial ultrasounds for fetal growth and amniotic fluid assessment².
- c. Placental Abnormalities and Placenta Accreta:** possibly due to uterine scarring from previous procedures or anomalies, especially with prior cesarean or uterine surgeries².
- d. Hypertensive Disorders:** Increased prevalence (up to 10-15%), potentially linked to abnormal placentation².
- e. Congenital Anomalies:** have been

reported with a slightly higher incidence (around 3-4%) compared to spontaneous pregnancies (~2-3%), possibly due to epigenetic influences or parental factors².

ANTENATAL CARE MANAGEMENT

Risk Stratification and initial assessment

Maternal demographics and history

1. **Advanced Maternal Age:** A significant proportion of ART patients are ≥ 35 years, increasing the risk for chromosomal abnormalities, hypertensive disorders, and gestational diabetes mellitus (GDM)³.
2. **History of Infertility:** The underlying etiology (e.g., diminished ovarian reserve, tubal factor, endometriosis, male factor infertility) and duration of infertility affects further pregnancy course and is associated with small for gestational age³.
3. **Pre-existing Comorbidities:** Higher prevalence of thyroid disorders, autoimmune conditions, and metabolic syndrome in ART populations.
4. **Medication History:** Use of gonadotropins, progesterone, and estrogen supplementation in the luteal phase and early gestation should be documented.

Detailed ART History and Documentation

1. Type of ART used:

Oocyte donation: Pregnancies resulting from oocyte donation have been associated with a higher risk of first trimester bleeding, miscarriage, gestational diabetes and pregnancy induced hypertension (PIH)⁴.

Gestational surrogacy: has a higher incidence of high birth weight as compared with autologous fresh IVF-ICSI cycle⁵. It is also associated with a higher risk of multiple gestation and preterm birth, which can be mitigated by the practice of single embryo transfer^{6,7}.

Fresh or frozen embryo transfer: When compared with fresh embryo transfer, frozen embryo transfer (FET) has an increased risk of large for gestational age in singleton pregnancy and a higher risk of PIH in case of a twin gestation⁸.

2. **Stimulation protocol and response:** In couples with PCOS and poor responders, when compared with agonist protocol, GnRH antagonists do not seem to compromise ongoing pregnancy rates and are associated

with less ovarian hyperstimulation syndrome (OHSS) and therefore could be considered as standard treatment⁹.

3. **Embryo quality and stage:** Fresh blastocyst-stage transfer is associated with higher rates of both clinical pregnancy and live birth rates, compared to fresh cleavage-stage transfer¹⁰.
4. **Use of preimplantation genetic testing (PGT)** and transfer of tested euploid embryos, or transfer of untested embryos.
5. **Single vs. multiple embryo transfer:** Single embryo transfer leads to decreased rates of multiple gestations with no significant impact on clinic-level live birth rates¹¹.
6. **Endometrial preparation details** in FET cycles can be done using an artificial cycle (by hormone replacement treatment, also known as HRT cycle) or in a 'more physiologic' non-stimulated endometrium in a natural or modified natural cycle. Natural cycle for endometrial preparation may not only result in higher pregnancy rates¹², but also potentially decrease maternal and neonatal morbidity.

Early Pregnancy Complications

1. **Ectopic pregnancy:** Even with intrauterine transfer, ART-conceived pregnancies have a higher ectopic risk (2–5%). Heterotopic pregnancy should be considered in symptomatic women.
2. **First-trimester bleeding or miscarriage** risk is elevated, particularly in older women or with poor embryo quality.

Surveillance Protocols

1. **First-Trimester Ultrasound:** Confirm viability, establish gestational age and document chorionicity and amnionicity in multiples.
2. **Need for luteal support:** Women undergoing hormonal support during early pregnancy (e.g., luteal phase support with progesterone or estrogen) needs close follow-up until placental autonomy is achieved (around 10–12 weeks).
3. **Genetic counselling and NIPT** is still recommended despite a euploid PGT-A result for confirmation.
4. **Anomaly Screening:** Consider detailed anatomical ultrasound at 18–22 weeks and fetal echocardiography in select cases as there is a higher incidence of congenital anomalies,

particularly in ICSI-conceived fetuses (especially urogenital and cardiovascular defects).

5. **Donor gamete cycles:** ART pregnancies, especially from donor gametes, may have increased immunological incompatibility, potentially contributing to higher preeclampsia and miscarriage rates.
6. **Fetal growth monitoring:** Every 4 weeks starting from 20 weeks, more frequent in multiple pregnancies or if growth restriction is suspected. Serial ultrasounds and regular umbilical artery and middle cerebral artery doppler studies in the third trimester may be warranted to assess for IUGR, and plan delivery based on gestational age and fetal condition.
7. **Placental Assessment:** Early and serial assessments for placental location and invasion signs, particularly in cases with previa or prior uterine surgery.
8. **Management of Multiple Pregnancies:** Counselling and discussion regarding the increased risks to babies, potential for preterm delivery, and need for neonatal intensive care.

Delivery Planning and intrapartum care:

Mode and Timing of Delivery: There is a tendency toward elective caesarean delivery in ART pregnancies, even in low-risk cases, driven by patient anxiety or provider caution. In uncomplicated singleton pregnancies, vaginal delivery is not contraindicated.

Delivery is generally recommended by 39–40 weeks unless otherwise indicated. In multifetal gestation or high-risk situations, individualized delivery planning is essential. In case of a preterm delivery, management with corticosteroids for fetal lung maturity is advised, and magnesium sulphate for neuroprotection.

Neonatal Considerations

Increased neonatal intensive care unit (NICU) admissions are reported in ART infants even after controlling for gestational age.

Psychosocial Aspects

ART patients often exhibit heightened anxiety and emotional investment in the pregnancy. Obstetricians should offer psychological support and communicate empathetically while managing complications or investigations. Shared decision-making is key in delivery planning and interventions.

Postpartum Considerations

Women should be monitored closely for postpartum hemorrhage, especially in cases with placental invasion. In addition to this, future pregnancy risks, including recurrence of complications and the importance of early prenatal care and the potential need for specialized obstetric care should be discussed. Appropriate contraceptive methods should be discussed, wherever required.

Conclusion

The obstetric care of women who conceive through ART requires a tailored, proactive, and evidence-informed approach. From a clinical standpoint, obstetricians must approach ART pregnancies with heightened surveillance and a multidisciplinary approach to antenatal care, emphasizing comprehensive antenatal care and personalized management strategies. Furthermore, psychological support is critical, as ART-conceived women often experience higher levels of anxiety related to pregnancy loss and complications, given the emotional and financial investment involved in achieving conception.

Ongoing research updated clinical guidelines, and continuous education of healthcare professionals are essential to optimize maternal and perinatal outcomes. Ensuring a safe pregnancy and delivery experience for this growing patient population is not only a medical necessity but also a responsibility shared by the broader reproductive and perinatal care community.

Referral Checklist:

1. Patient & Clinic Information

Patient Name: _____

Date of Birth: _____

Referring IVF Clinic: _____

Referring Physician: _____

Clinic Phone: _____

Clinic Fax/Email: _____

Date of Referral: _____

2. ART Cycle Details

ART Procedure Used:

☐ IVF

☐ ICSI

☐ Other: _____

Oocyte (Egg) Source:

☐ Autologous (Patient's own)

☐ Donor

Sperm Source:

☐ Autologous (Partner's own)

☐ Donor

Number of Embryos Transferred:

Number of Gestational Sacs Seen on Final Scan: _____

Preimplantation Genetic Testing (PGT):

☐ Not Performed

☐ PGT-A (Aneuploidy): Result ☐ Euploid ☐ Other: _____

☐ PGT-M (Monogenic): For condition:

☐ PGT-SR (Structural Rearrangement)

3. Pregnancy Dating & Viability Confirmation

The Last Menstrual Period (LMP) is not a reliable indicator for this pregnancy.

Date of Embryo Transfer:

Type of Transfer:

☐ Fresh Embryo Transfer

☐ Frozen Embryo Transfer (FET)

Age of Embryo at Transfer:

☐ Day 3

☐ Day 5 (Blastocyst)

☐ Day 6

☐ Other: _____

Adjusted LMP = Transfer date- [embryo age in days e.g. Day 3 or day 5 embryo] + 14 days]

Examples:

1. Day 5 blastocyst transfer on 10 September 2025

Adjusted LMP= 10 Sept- (5+14) days = 22 August 2025 (here embryo age= 5 days)

2. Day 3 cleavage stage transfer on 10 September 2025

Adjusted LMP = 10 Sept- (3+14) days = 24 August 2025 (here embryo age = 3 days)

Calculated gestational age (using adjusted LMP): _____

Estimated Due Date (EDD):

Early Pregnancy Milestones:

* First Positive hCG:

* Date: _____

* Value: _____ mIU/mL

* Second hCG (if done):

* Date: _____

* Value: _____ mIU/mL

* First Ultrasound:

* Date: _____

* Findings: Gestational Sac(s): __ Yolk Sac(s): __

* Viability Ultrasound:

* Date: _____

* Findings: Fetal Pole(s) Seen: __ Fetal Heart Rate(s): _____

4. Relevant Medical & Gynecological History

Primary Fertility Diagnosis:

☐ Maternal ☐ Paternal ☐ Unexplained ☐ Other

Details: _____

Relevant Maternal History:

☐ PCOS

☐ Endometriosis

☐ Diminished Ovarian Reserve

☐ Uterine Anomaly (e.g., Septate, Bicornuate):

☐ Recurrent Pregnancy Loss

☐ Fibroids

☐ Hypertension

☐ Thyroid Disorder

☐ Diabetes

☐ Autoimmune Condition

Previous Obstetric History (G/P/A): G: __ P: __
(Term: __ Preterm: __) A: __ L: __

OHSS in cycle?

☐ No

☐ Yes (Severity: ☐ Mild ☐ Moderate ☐ Severe)

5. Additional Information & Recommendations

Previous ART cycles and outcomes:

Lifestyle Factors (smoking, alcohol, etc.):

Specialist Consultations or Recommendations:

6. Current Luteal & Hormonal Support Plan

Patient has been instructed to continue the following medications until advised otherwise by you.

- * Progesterone:
- * Dose & Route: _____
- * Suggested Stop / Taper Date: _____
- * Estradiol:
- * Dose & Route: _____
- * Suggested Stop / Taper Date: _____
- * Low-Dose Aspirin (81 mg):
- * Dose & Route: _____
- * Suggested Stop / Taper Date: _____
- * LMWH / Anticoagulant:
- * Dose & Route: _____
- * Suggested Stop / Taper Date: _____
- * Other (e.g., Steroids, etc.):
- * Dose & Route: _____
- * Suggested Stop / Taper Date: _____

7. Key Considerations & Recommendations for Obstetrician

☐ Increased Risk for Multiples: Note that ____ embryo(s) were transferred. Please monitor for late appearance of additional sacs.

☐ Consider Early Screening: This pregnancy may be at a higher baseline risk for pre-eclampsia, GDM, and placental abnormalities.

☐ Cervical Length Monitoring: Consider serial cervical length screening, especially in cases of multiple gestations or previous uterine surgery.

☐ Genetic counselling

☐ NIPT is still recommended despite a euploid PGT-A result for confirmation.

☐ Further diagnostic testing (CVS/Amnio) should be discussed based on PGT results and maternal history.

☐ Other Pertinent Information:

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Tricky Situations in Ovarian Stimulation in IUI Cycles



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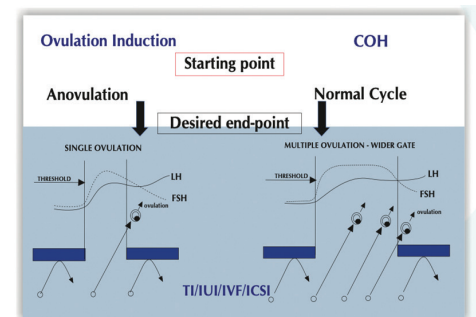
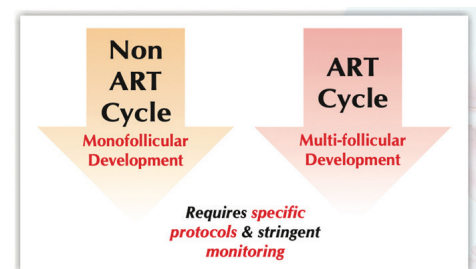
Intrauterine insemination with ovarian stimulation (IUI-OS) is a first-line treatment for couples with unexplained infertility.¹ It aims to increase the pregnancy rates by increasing the number of dominant follicles per cycle, which is achieved by increasing the serum levels of FSH.² Agents which increase FSH serum levels include exogenous gonadotrophins, letrozole or clomiphene citrate (CC). Gonadotrophins have a direct effect on follicle growth as they contain FSH and may also contain recombinant LH- or HCG-driven LH activity. Letrozole is a third-generation aromatase inhibitor that interferes with the oestrogenic feedback at the pituitary by blocking oestrogen biosynthesis thus stimulating the production of serum FSH.³ CC is a selective oestrogen modulator and competes with oestrogen for binding to the hypothalamic oestrogen receptors, thus stimulating the production of serum FSH (3). While letrozole and CC are orally taken for 5 days, the gonadotrophins are injected subcutaneously.⁴

When is OS required in an IUI cycle?

- In couples with unexplained infertility and male partner with a TMSC above 10 million, IUI should be combined with OS to improve live birth rates.
- In couples with unexplained infertility and men with a TMSC > 10 million and a prognosis of spontaneous pregnancy <30% based on Hunault's score within a year, it is recommended that IUI plus OS are the treatments of first choice.⁵

The basis of this approach is to "simply increasing the number of gametes at the site of fertilization" might increase the likelihood of conception.

1. The rationale of OS is to achieve multifollicular growth.² showed that multifollicular growth resulted in significantly higher pregnancy rates compared to monofollicular growth (15 versus 8.4%). Compared to one dominant follicle, pregnancy rates increased by a further 5, 8 and 8% when two, three or four dominant follicles were present, respectively.²
2. For unexplained infertility, the Cochrane systematic review of (6) showed us that IUI without OS does not positively influence pregnancy outcomes. Adding OS to IUI significantly increases live birth rates in couples with unexplained infertility. Although, OS is a well-known risk factor for (high order) multiple pregnancy.



Tricky situations which can arise in this scenario include

- A. Multiple follicular development
- B. Premature LH surge with gonadotropin therapy
- C. Semen sample collected exhibited low semen quality

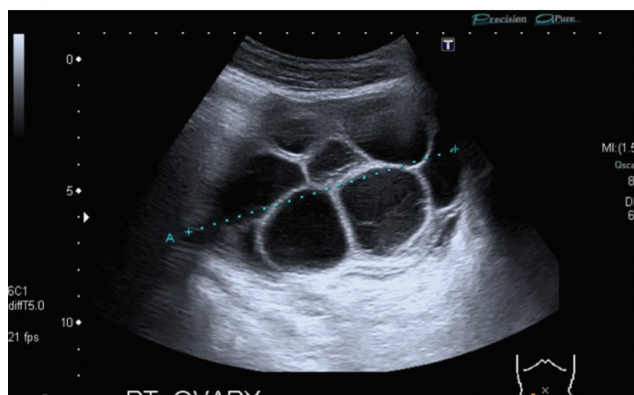
A. Multiple follicular development

Though the development of multiple follicles increases the chances of pregnancy manifold, high multiple birth rates present a substantial problem.

After a Finnish study pointed out that the rates of multiple pregnancy can be reduced by transferring a single embryo, most countries have moved to the SET policy in IVF cycles. But in IUI cycles, that option is not available.

Therefore, an optimal OS+IUI strategy should aim to increase cumulative CBR without increasing the multiple pregnancy rate.

The presence of multiple follicles is a key predictor of multiple gestation, and risk increases with the number of follicles greater than 10-14 mm in diameter.



Primary prevention

To avoid multiple pregnancies and OHSS, ESHRE unexplained infertility guideline¹ suggests using a low-dose gonadotropin regimen with adequate monitoring.

Decision for the dose of Gonadotropin depends upon the following factors-

- 1) Age
- 2) BMI
- 3) Ovarian reserve
- 4) Previous ovarian response help clinicians to decide the dose of gonadotropin

The usual aim is to develop 2-3 dominant follicles. However, there could be a situation where the response overshoots the expectation and there are >3 dominant follicles

Starting dose of gonadotropin

Tuq et al ⁷and Gleicher et al (8) have demonstrated that doses exceeding 150 IU increased the risk of multiple pregnancy. After a thorough evaluation of evidence, ESHRE recommends a low-dose gonadotropin for ovarian stimulation in IUI cycles.

ESHRE(1) recommends:

- 1. When gonadotropins are used in an IUI regimen, 75IU or lower should be used
- 2. CC or tamoxifen are acceptable alternatives to low-dose gonadotropin.

Secondary prevention

If there is a multifollicular development of >3 DF (of size 13-15mm), strategies need to be in place to tackle this tricky situation.

1. Cancellation of cycle /withholding the cycle

ESHRE(1) has suggested that IUI should be withheld when more than 2 DF>15mm or more than 5 follicles >10mm at the time of HCG injection or LH surge are present.

2. Aspiration of follicles

Alternative to cycle cancellation, aspiration of excess follicles at the time of HCG Injection might be an additional option.

3. Conversion to IVF

It is proposed that high response IUI cycles may be converted to low cost IVF as a method to decrease the chances of multiple pregnancy and OHSS

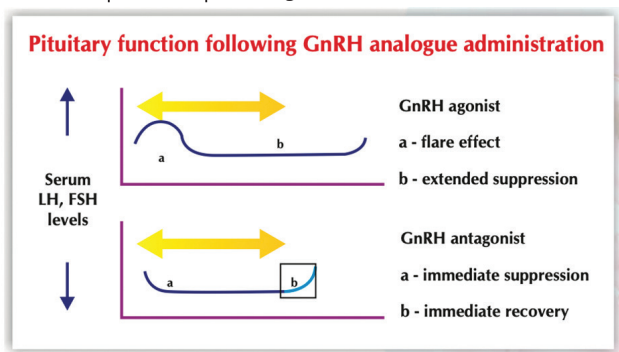
In 2012, Zhong et al (9) studied the efficacy of conversion from IUI to IVF ET in patients with hyper- response to ovulation induction and found it to be an effective method to prevent multiple pregnancies and OHSS

B. Premature LH surge with gonadotropin therapy

Adjuvant drugs to prevent premature LH surge

- GnRH agonists in combination with hMG and/or FSH
- GnRH antagonists in combination with hMG and/or FSH protocol

Though LH surge is an absolute requirement for luteinization, final maturation of the oocyte and follicle rupture but a premature LH surge can occur in natural cycle and in 25 – 30% of stimulated cycles resulting in premature luteinization of follicle, early rupture of follicle so that exact time of ovulation is missed resulting in treatment failures in an timed intercourse and IUI cycle. A premature LH surge is defined as premature rise of LH ($>10\text{IU/l}$) accompanied by concomitant rise in progesterone levels ($>1\text{mg/l}$).¹⁰ So we need to see whether use of GnRH agonist or antagonist in IUI cycles is a cost effective and helps in improving the outcome.



GnRH agonists in ovarian stimulation for IUI

There seems to be no role for GnRH-agonists in IUI programs as they increase cost as the dose of gonadotrophins is increased tremendously. Its use also increases the incidence of multiple pregnancy without increasing the probability of conception. Thus use of GnRH agonists with gonadotrophins should be carefully considered in an intrauterine insemination program.¹¹

GnRH antagonists in ovarian stimulation for IUI

When GnRH antagonists are used for ovarian stimulation in combination with there may be a small increase in probability of pregnancy. They may be helpful in cycle programming and avoidance of inseminations during weekends. Conversion of high-response gonadotropin-IUI cycles to "rescue" IVF using a GnRH antagonist is a cost- effective strategy that produces better results than regular IVF with relatively minimal morbidity, and shorter duration to achieve pregnancy. Implantation and ongoing clinical pregnancy rates tend to be higher than those from hyper-responder regular IVF patients. Whether or not GnRH-antagonists should be used regularly in IUI programs needs to be determined in future trials.¹¹

But what to do if the LH surge happens before we give the trigger?

We need to understand that

- Sperms can remain in the female tract for up to 5 days.
- Ovulation happens about 24-36 hours after the initial rise in LH.
- Once ovulation happens, the egg can only survive for up to 24 hours.
- If insemination (either IUI or ICI) takes place within 48 hours of the LH surge, the timing of the procedure will not influence the probability of conception.

Pregnancy rates were found to be comparable when IUI is performed 24 or 48 hours following spontaneous LH peak in a randomised controlled trial.¹²

C. Semen sample collected exhibited low semen quality

The most recent version of the WHO manual¹³ recommends 2-7 days of abstinence. However, this has been recently challenged. Several studies demonstrated that the second successive samples exhibited significantly improved progression motility and reduced sperm DNA fragmentation. Study suggests a successive semen sample obtained 1 to 4 hours after the first does not necessarily exhibit reduced sperm concentration or TMSC and may even have better parameters. Therefore, obtaining a second successive semen sample in certain cases, especially in men who present on the day of IUI with a low-quality sample, might be a rational course of action.¹⁴

Conclusion

Intrauterine insemination with ovarian stimulation (IUI-OS) is a critical treatment for couples with unexplained infertility, aiming to enhance pregnancy rates by increasing the number of dominant follicles. While multifollicular growth significantly boosts pregnancy chances, it also raises the risk of multiple pregnancies, necessitating careful management and monitoring. Strategies such as low-dose gonadotropin regimens, cycle cancellation, follicle aspiration, and conversion to IVF are essential to mitigate these risks. Additionally, addressing premature LH surges and optimizing semen quality are crucial for improving treatment outcomes. Overall, a well-balanced approach to IUI-OS can maximize success rates while minimizing potential complications.

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Should Preimplantation Genetic Testing be Offered to Women with Recurrent Pregnancy Loss



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Introduction

Recurrent pregnancy loss(RPL) is one of the most distressing obstetrics complication which is defined as loss of two or more consecutive and nonconsecutive pregnancy losses before 20-24 weeks which now incorporates biochemical pregnancy as well.^{1,2} However Royal College of obstetrics and Gynecologist (RCOG) defined RPL as loss of three or more pregnancy loss but left the decision of extensive evaluation of couple on clinical discretion after the two losses.³ The prevalence reported in literature was 0.8% to 1.4% when only clinical miscarriages (as verified by histology and/or ultrasound) were taken into the account; the frequency has now risen to 2% to 3% when biochemical losses are added.⁴ Majority of the couple considers pregnancy loss as a very emotional distressing event and felt a lot of grief which gets exuberates after repeated loss.⁵

To determine the reason behind pregnancy loss is crucial for couples and is essential for the treatment of their upcoming pregnancy. There are certain well known causes have been identified which includes uterine structural malformation, certain endocrinological disorder (Thyroid disorder, Diabetes, Hyperprolactinemia), APLA (Anti-phospholipid antibody)syndrome and parental structural chromosomal rearrangements but still these causes can explain the loss in only 42.9% of couples, and over half of the cases are still unaccounted for, categorized as unexplained RPL.^{2,6} Recent advances in genetic testing of the products of conception (POC) using 24 chromosomal microarray have raised awareness of the part aneuploidy plays in RPL and came in to a light as a major cause of RPL, especially in a women of advance age(>35years).(5-7) Genetic testing of product of conception along with other recommended tests for might help us to identify the probable or certain cause of miscarriage in 90% of the cases and help us to decide subsequent course.^{6,7}

Sometimes genetic testing results of parents or product of conception may warrant the use of Pre-implantation genetic testing (PGT) as the further course of management. Pre-implantation genetic testing (PGT) is a known genetic testing which necessitates using Artificial Reproductive Technique (ART) which includes IVF or ICSI and then the biopsy of an embryo subsequently. It has been used to detect a variety of genetic conditions, and the testing includes

1. PGT-SR- For identifying chromosomal structural rearrangements,
2. PGT-A-For detecting common aneuploidies (PGT-A) and
3. PGT-M- It is used to detect certain monogenic conditions (PGT-M).

Methods of PGT

There have been significant advancements in the platforms for thorough chromosomal screening in PGT which initially used polymerase chain reaction (PCR), fluorescent in situ hybridization (FISH) thereafter soon replaced by array comparative

genomic hybridization (aCGH), single nucleotide polymorphism (SNP) array for finer diagnosis and recently next-generation sequencing (NGS).^{7,9} The ability to detect triploidy with SNP microarrays is superior to array comparative genomic hybridization while NGS have higher mosaicism detection rate when compared to SNP.^{8,9}

In current literature NGS when compared to aCGH and SNP have been found to have low miscarriage rate and higher live birth rate (LBR).^{8,10} So, it is now preferred and most common used platform for genetic analysis in PGT, because of its low cost and wide application. By whole genome sequencing, it helps detecting aneuploidy along with monogenic disorders and unbalanced translocations as well.^{8,11}

Current Recommendations and literature for PGT in RPL-

PGT-SR

Pre-implantation genetic testing as PGT-SR has well established application in RPL in those where balanced parental translocation (reciprocal and robertsonian) has been identified in parents or unbalanced translocation or inversion has been found during genetic testing of product of conception. Although the choice between expectant management or PGT-SR has to be made after proper genetic counseling of the couple, but mostly in these scenarios it is recommended to offer ART with PGT-SR to decrease the miscarriages and time to achieve live healthy birth. In some scenarios when couple carrying a balanced chromosomal rearrangement involving imprinted genes (e.g., 13;14 Robertsonian translocation), chorionic villus sampling/Amniocentesis can also be offered later in pregnancy to rule out problems linked to uniparental disomy, as preimplantation genetic testing analysis techniques cannot rule out the rare occurrence of these conditions.^{1,12,13}

PGT-A

PGT-A on the other hand, which is designed to detect chromosomal aneuploidy which occur sporadically in embryo and can be a reason of recurrent pregnancy loss, has varied data in literature regarding its application in RPL and not recommended as a standard norm till now due to absence of high quality evidence.^{1,3,12} Earlier study conducted by Kort et al and Liu et al suggested higher aneuploidy rate in unexplained RPL, though the study population and the statistical analysis of the studies are questioned by a recent meta-analysis conducted by Mumusoglu et al.¹⁴⁻¹⁶ Still aneuploidy is considered as the primary cause of early pregnancy losses and it increases with the age is well known fact⁹, which warranted to assess

the role of PGT-A as potential management option in particular group of RPL patients

Initially Murugappan et al. (2016) showed no improvement in outcomes when comparing expectant care without IVF to women with RPL using PGT-A with IVF in a retrospective cohort analysis.⁽¹⁷⁾ However, this study was later critically reviewed for the bias caused by the difference in the age group between two groups as well as to exclude the couple with low embryo quality and it was suggested that PGT-A should be used for couples with low embryo quality; hence, notwithstanding the findings of the Murugappan trial, it was proposed that PGT-A may still be useful in couples with RPL.¹⁸ In another study when compared to standard IVF, PGT-A for patients with RPL due to embryonic aneuploidy was linked to a higher LBR per embryo transfer, but not per patient as there was significant number of patients lacked a viable euploid embryo, which prevented them from progressing to the embryo transfer stage. The same study also stated reduced biochemical pregnancy in RPL group in IVF-PGT-A patients.¹⁹

Later on one of large study conducted by Bhatt et al comparing pregnancy outcome in IVF following PGT-A and non PGT-A embryo transfer in RPL patient found increased live birth and clinical pregnancy rate along with the decrease in miscarriage rate in women with tested embryo. They also noticed the markedly in change in the women with more advance age.²⁰ This study further supported by other further large studies and systemic reviews.^{9,16,21}

Currently, none of the major societies (ESHRE, ASRM and RCOG) justify the regular use of PGT-A in individuals with unexplained RPL and still recommend an expectant management for unexplained RPL (1-3). Though for genetic for analysis of POC's, RCOG has recommended it after third miscarriage and ESHRE stated it can be done for explanatory purpose considering aneuploidy as an major cause of pregnancy losses and its risk increases with age.^{1,3}

However the recent literature which includes very latest systemic review and meta-analysis by Mumusoglu et al supported the use of ART with PGT-A in unexplained RPL, especially in certain group of patients. As per these studies couples with unexplained RPL (as per ASRM and ESHRE criteria) with a history aneuploidy pregnancy loss or advance maternal age can be a candidate for ART with PGT-A consideration as it enhances the live birth rate and reduces the pregnancy loss rate.^{16,20,21}

Limitations with using PGT in RPL

The role of PGT has long been in controversial,

due to its some limitations. First of all it always requires an ART (IVF & ICSI) procedure sometimes in otherwise fertile women also which increases the cost of procedure without the certainty of positive results. Secondly it's a highly skilled procedure which involves taking a biopsy from the trophoectoderm part of blastocyst and it requires a highly skilled personal in a good ART facility to perform otherwise it might damage the embryo or can give the unsatisfactory results. The other major concern is the misdiagnosis or reporting of mosaic embryo which can result in discard of embryo that could have the potential giving healthy live birth especially with the low level of mosaicism.²² This limitation mandates the use of good genetic laboratory for the analysis and assessment. Henceforth, further more large randomized trials and robust evidence can help PGT-A to establish its role in unexplained recurrent pregnancy loss more firmly.

Recent advances in PGT (niPGT-Non-invasive PGT)

New opportunities for noninvasive embryo aneuploidy testing in assisted reproductive technologies have been made possible by the discovery of embryonic cell-free DNA in discarded blastocyst medium. In addition to potentially

overcoming technological limitation, this can mitigate the effects of invasive embryo biopsy, reduce expenses, possibly making PGT accessible to more patients.²³

Recent literature has shown it as a promising tool with concordance in the genetic analysis result as well as in clinical outcome.²³⁻²⁵ Still, it needs a more research to replace trophoectoderm biopsy in PGT testing as a standard protocol.

Conclusion

ART(IVF&ICSI) with PGT-A in good hands with good embryology and genetic laboratory can help the couple to reduce the time and number of pregnancy loss which they might have to bear to achieve one live birth, especially in a couple with RPL having an advance age of female, considering aneuploidy as a most common reason for miscarriage in them. It should definitively be individualized depending on the patient choices, ovarian reserve, procedure risks and cost effectiveness (Figure 1 and 2). There should also a focus on genetic testing of fetus in unexplained RPL for the explanatory purpose as miscarriages can be very emotional exhausting for the couple and also it might also help to form an informed and well discussed mutual plan for the future management for the couple.

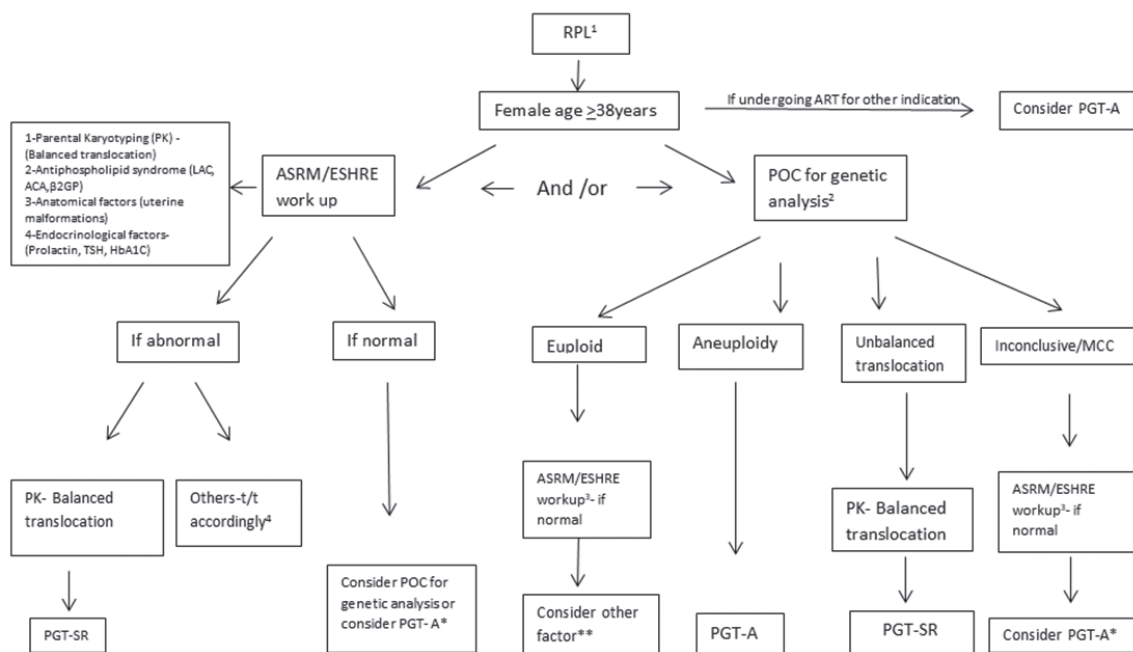


Figure 1- Algorithm to manage RPL in Female age ≥ 38 year

- 1- Pregnancy loss of 2 or more consecutive and nonconsecutive pregnancy before 20-24 weeks
 - 2- Genetic analysis of product of conception using chromosomal microarray (can be done with or before APLA/ESHRE work up)
 - 3- If work up already not done
 - 4- Treatment as per the ASRM/ESHRE guideline- APS-anticoagulant prophylaxis, consider optimizing anatomical and endocrinological factors.
- *Consideration of PGT-A should be individualized, other factors should be considered (patient choice, ovarian reserve, cost, success)
 **Individualized plan should be form, before considering other any under research investigations (Hereditary thrombophilia, DNA fragmentation, allg-immune factors) and treatment (Intravenous immunoglobulin, lymphocyte immunization therapy, anticoagulant) in view of scarcity of literature. Optimization of lifestyle can be considered in all cases.
 ESHRE- European Society of Human Reproduction and Embryology, ASRM-American Society of Reproductive medicine

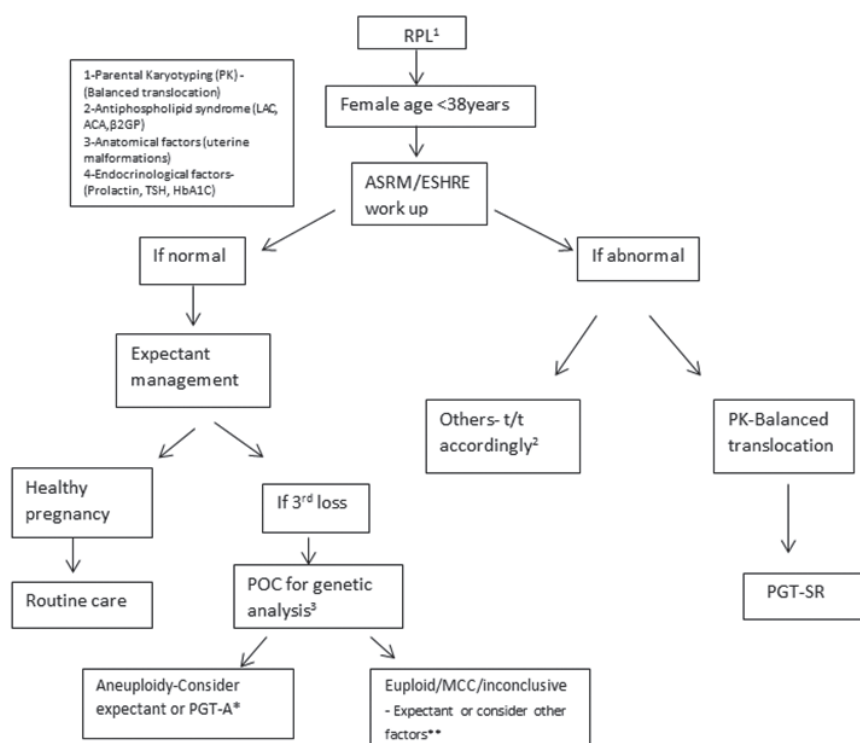


Figure 2- Algorithm to manage RPL in Female age<38 year

1- Pregnancy loss of 2 or more consecutive and nonconsecutive pregnancy before 20-24 weeks

2- Treatment as per the ASRM/ESHRE guideline- APS-anticoagulant prophylaxis, consider optimizing anatomical and endocrinological factors.

3- Genetic analysis of product of conception using chromosomal microarray.

*Consideration of expectant management and PGT-A should be individualized, other factors should be considered (patient age, choice, ovarian reserve, cost, success)

**Individualized plan should be formed, before considering other any under research investigations (Hereditary thrombophilia, DNA fragmentation, and allo-immune factors) and treatment (Intravenous immunoglobulin, lymphocyte immunization therapy, anticoagulant) in view of scarcity of literature. Optimization of lifestyle can be considered in all cases.

ESHRE- European Society of Human Reproduction and Embryology, ASRM-American Society of Reproductive medicine

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Management of Androgen Excess in the Adolescents



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Androgen excess may affect a varying number of adolescents. The most common symptoms are hirsutism and acne, both of which have a tremendous psychological impact in this population.

In patients with symptoms of androgen excess, the differential diagnosis should include

- Physiological hyperandrogenism of puberty
- Idiopathic hyperandrogenism
- PCOS

Other less common potential causes of hyperandrogenism include

- NCCAH (Non classical CAH)
- Androgen secreting tumors
- Hypothyroidism
- Cushing disease

Polycystic ovarian syndrome in adolescents

Polycystic ovary syndrome is the most common cause of persistent hyperandrogenism beyond early puberty in adolescent girls and women and is estimated to affect 6-15% of reproductive-aged women. In this syndrome, chronically elevated luteinizing hormone and insulin levels lead to increased androgen production within the ovarian theca. There is a great deal of overlap between the symptoms of PCOS and those of normal puberty (eg, irregular menses, acne, polycystic ovarian morphology on ultrasonography), which makes the diagnosis of PCOS in the adolescent difficult.

There are no clear consensus guidelines on the diagnostic criteria for PCOS in adolescent

girls within 2 years of menarche; thus, gynecologists should exercise caution in assigning this diagnosis prematurely. Most experts agree that longitudinal evaluation of symptoms such as acne, hirsutism, and oligomenorrhea should occur over the span of the first 1-2 years after menarche before establishing a diagnosis of PCOS. PCOS exists along a spectrum that may evolve over time and can present differently among different ethnicities. However, treatment of acne and hirsutism should not be withheld during the ongoing longitudinal evaluation for possible PCOS. In addition, although obesity and insulin resistance are not diagnostic criteria for PCOS, they often co-exist in this population and warrant early counseling on healthy weight, nutrition, exercise and evaluation to exclude diabetes.

ESHRE 2023 guideline on PCOS 2023 quotes that 'For adolescents who have features of PCOS, but do not meet diagnostic criteria, an 'increased risk' could be considered and reassessment advised at or before full reproductive maturity, 8 years post menarche. This includes those with PCOS features before combined oral contraceptive pill (COCP) commencement, those with persisting features and those with significant weight gain in adolescence.'

Evaluation of the Hyperandrogenic Adolescent

History: Age of thelarche, adrenarche, and menarche; past laser hair removal or shaving; off-label use of anabolic steroids or testosterone; and menstrual history, including frequency and duration should be

asked for . The timing and progression of acne and hirsutism, along with a record of previous therapies, are helpful for management. A history of rapid onset of virilization (deepening of the voice or frontal balding) is more concerning for androgen secreting tumors. If obesity is present, timing and progression of weight gain should be assessed.

Family history of hirsutism, severe acne, PCOS, or obesity also should be recorded.

Examination: BMI, BP, acne, hirsutism, signs of insulin resistance (centripetal fat distribution, skin tags, acanthosis nigricans).

Hirsutism: Modified Ferriman Galleway score – score >8 is indicative of hirsutism.

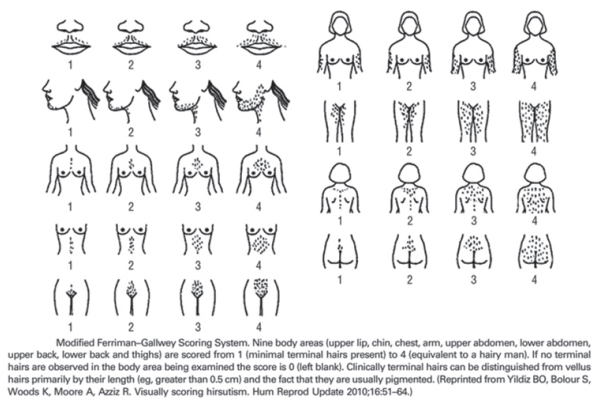
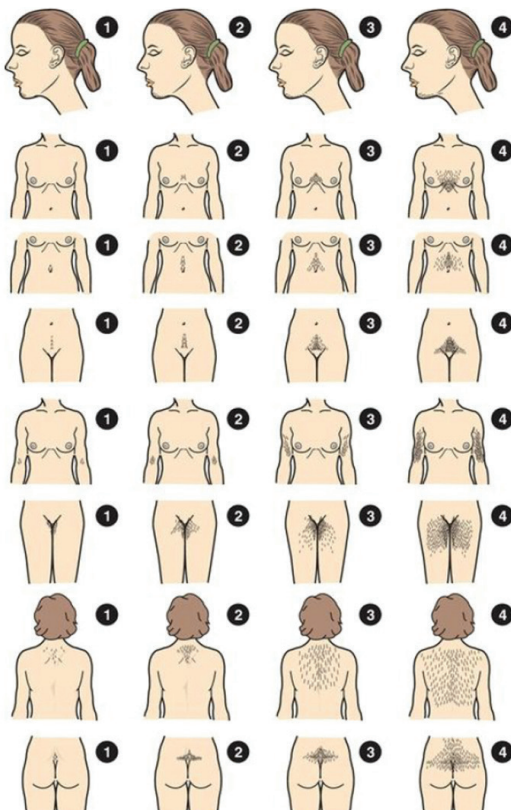


Figure 1: Modified Ferriman-Galleway Scoring system.



Acne: Grading systems for acne include quantity (mild, moderate, or severe), location, and quality (comedonal, inflammatory [including erythematous papules and pustules or nodules], or mixed). There is no universally agreed upon grading scale.



Figure 2: Severe grades of acne.

Female Pattern Hair Loss (FPHL): FPHL is a thinning of hair primarily in the sagittal area of the scalp, caused by miniaturization of the hair follicles (a process whereby the scalp terminal hairs become smaller and eventually become short vellus hairs). There are two common pattern types of FLP in women. Ludwig described diffuse hair thinning in the centroparietal region with a preserved frontal line. In contrast, the 'Christmas tree' pattern is associated with diffuse centroparietal thinning of the hair in conjunction with branching of the frontal hair line. FPHL is a process generally characterized by an increase in the proportion of scalp hairs that are in telogen (i.e. lying unattached from the follicular bulb within the hair shaft ready to be extracted/shed), a finding that can be assessed by the 'hair-pull test'.



Figure 3: Christmas tree appearance of female pattern hair loss.

External examination of the genitalia: rule out clitoromegaly. Although there is variability, for adolescents aged 13-16 years, clitoromegaly is diagnosed when the clitoral index (width x length) exceeds 35 mm².

Pelvic ultrasonography: Not routinely indicated

unless serum androgen levels or the degree of virilization is concerning, to rule out an ovarian tumor.

Investigations

The diagnosis of hyperandrogenism can be based on clinical symptoms or measurement of serum androgens. In females, androgens originate from three primary sources:

1. the ovarian theca,
2. the adrenal cortex, and
3. within end organs by peripheral conversion.

The major androgens include dehydroepiandrosterone, dehydroepiandrosterone sulfate (DHEAS), androstenedione, testosterone, and dihydrotestosterone, with the latter two having the highest affinity for the androgen receptor and the greatest potency. In healthy women, testosterone is largely bound by sex hormone binding globulin and albumin, leaving only approximately 1% freely circulating as bioactive "free testosterone".

First line hormonal tests– total testosterone, free testosterone and 17 OHP.

Total testosterone can be affected by diurnal rhythms, phase of menstrual cycle, and sex hormone binding globulin concentrations. Laboratory use of high-quality radioimmunoassays are recommended rather than enzyme-linked immunosorbent or chemiluminescent assays, which have poorer sensitivity. Normal value is between 20 to 80 ng/ml. Levels greater than 150 ng/dL are suggestive of a virilizing tumor and should prompt pelvic ultrasonography. Total testosterone is often preferred for initial evaluation because free testosterone assays are frequently unreliable.

Free testosterone may be a more direct indicator of potential symptoms of androgen excess, such as those seen in PCOS. Measuring free testosterone (or calculating the free androgen index (FAI)) can provide a more accurate picture of androgen levels in women than total testosterone alone, especially when diagnosing hyperandrogenism.

Ideally, blood should be drawn for the serum 17-hydroxyprogesterone test in the morning. In chronically anovulatory women with evidence of hyperandrogenism, a follicular phase morning serum 17-OHP concentration less than 200 ng/dL excludes, and a level greater than 800 ng/dL all but establishes the diagnosis of late-onset CAH due to 21-hydroxylase deficiency. Concentrations between the two threshold values suggest the possibility, which can be confirmed by performing an ACTH stimulation test, obtaining blood samples before

and 60 minutes after administering cosyntropin (synthetic ACTH; 0.25 mg intramuscularly or intravenously); in most women with nonclassical CAH, the 17-OHP concentration will rise above 1,500 ng/dL. Testing for DHEAS may be done to rule out adrenal neoplasm; this may be appropriate in cases of rapid onset of virilization.

Computed tomography or ultrasonography to evaluate the adrenal glands should be obtained for patients with markedly elevated DHEAS levels. Adolescents with suspected PCOS should be screened for diabetes and hyperlipidemia.

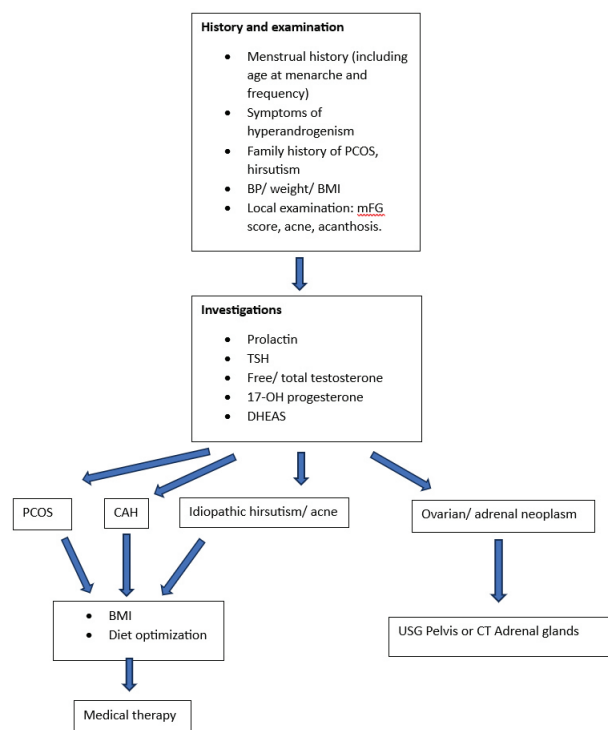


Figure 4: Management of hyperandrogenism in adolescents.

Management

Management aspect of hyperandrogenism in adolescent girls has two aspects – acne and hirsutism. The underlying cause of these manifestations should be looked for first (i.e. PCOS, adrenal gland) and treated.

Management of Hirsutism

Initiation of treatment should be based on the patient's perception of the problem, rather than quantitative characteristics of hirsutism. Multimodal therapy is the most effective approach to the treatment of hirsutism; this includes lifestyle changes, physical hair removal, and androgen suppression or blockade with medication that slows or prevents new hair growth. Patients also should be counseled that given the life span of terminal

hair, 6 months of medical therapy is required before slower and finer regrowth of hair is noted.

1. **Lifestyle changes:** The prevalence and degree of hirsutism is higher among obese girls with PCOS. Abdominal obesity, associated with PCOS, leads to increased insulin levels, and reduced hepatic synthesis of the sex hormone binding globulin (SHBG). This in turn causes an increase in free androgens concentration. In adolescents, focus should be prevention of excess weight gain. According to ESHRE, adolescents should aim for at least 60 minutes of moderate- to vigorous-intensity physical activity per day including activities that strengthen muscle and bone, at least three times per week.
2. **Oral contraceptive pills (OCPs) :** Progestins in OCPs causes suppression of LH levels and inhibition of LH-mediated ovarian androgen synthesis. The contained ethinylestradiol leads to a significant increase in SHBG, thus contributing to a reduction of Free Testosterone. Moreover, OCPs modestly affect adrenal steroidogenesis by decreasing the synthesis and release of androgens. Commonly reported side effects include nausea, bloating, mood changes, and breakthrough bleeding. According to ESHRE, OCP's could be considered in adolescents at risk or with a clear diagnosis of PCOS for management of hirsutism and/or irregular menstrual cycles. Among the formulations, OCPs that contain third-generation progestins, such as desogestrel, gestodene, and norgestimate, have less androgenic activity when compared with second-generation progestins (levonorgestrel). Drospirenone, a progestin derived from spironolactone, has antimineral corticosteroids and antiandrogenic properties and is frequently used to treat hirsutism. COCPs with 35ug EE and cyproterone acetate should not be used first-line and are indicated for treating moderate or severe hirsutism or acne, due to higher risk for venous thrombosis.
3. **Antiandrogens:** Antiandrogens generally include two Androgen receptor -blockers, spironolactone and flutamide, and one 5 α -RA inhibitor, finasteride. While the side-effects of antiandrogens vary some, there are two side-effects and risks that are common to all. Firstly, all antiandrogens are teratogenic, in that they may cause feminization of the genitalia in a male fetus. Secondly, they all have the potential to cause side-effects related to their

antiandrogenic properties, including some muscle weakness. In general, because efficacy is generally higher when using a combination of OCPs and antiandrogens, and because OCPs minimize the risk of teratogenicity, we generally begin therapy with a combination of OCPs and antiandrogens.

Spironolactone is approved for the treatment of hirsutism and works as a competitive inhibitor of the androgen receptor and 5 α -reductase inhibitor. It also is an aldosterone antagonist. Typical doses for the treatment of hirsutism range from 50 to 200 mg daily.

Other antiandrogens, such as flutamide and finasteride, have demonstrated a similar efficacy to spironolactone, but are used less commonly because of the potential for hepatotoxicity.

4. **Physical/Chemical methods:** Short-term mechanical methods include shaving, chemical depilation, plucking (threading), waxing, and bleaching; long-term mechanical methods include electrolysis, laser therapy, and intense pulse light (IPL) therapy. In addition, a 13.9% topical solution of eflornithine hydrochloride (HCL) can be used to reduce facial hair growth, although its effect is short-term and requires daily use. Eflornithine hydrochloride acts as permanent inhibitor of enzyme ornithine decarboxylase, which is required for the growth and differentiation of cells in the hair follicle. Topical administration of eflornithine HCL was shown to slow facial hair growth. This action is reversible and hirsutism relapsed after eight weeks of cessation of treatment. The general use of eflornithine HCL is not approved for large surface areas of the skin due to systemic effects; therefore, its use should be restricted to the removal of facial hair only.

Management of Acne

A variety of therapies can be used to treat acne in adolescents. As with hirsutism, multimodal approach is favorable, and response to therapy may take several months. Working with a dermatologist can be beneficial for patients with moderate-to-severe acne or acne refractory to initial medical therapy. Referral to a dermatologist should be made for complex cases. Treatment options:

1. **Topical therapy:** Topical therapy includes medications that are available over-the-counter or by prescription. The type of topical therapy can be influenced by affected site, severity of

disease, or patient preference. Topical agents can be used alone, with other topical therapies, or in combination with oral agents. Patients also may have concerns about skin sensitivities to various topical agents, and often a dose escalation regimen can be used for tolerability (eg, applying the medication every other night for 1-2 weeks before advancing to every night). The type of agent and patient skin type also should be considered; for example, patients with oily skin may prefer gels or solutions, whereas those with drier skin may prefer creams.

- 2. OCPs:** Hormonal therapy is an acceptable first-line approach to management of acne for adolescents. This approach may be particularly appealing to adolescents who are also interested in menstrual cycle control, contraception, or both. Any estrogen-containing therapy should be effective at reducing acne, and OCPs particularly are effective for adolescents who report premenstrual acne flare-ups. Although progestins vary in their androgenic potential, when combined with the effects of ethinyl estradiol, the net effect of all OCPs is antiandrogenic. However, for patients who do not show improvement on first or second generation progestins, a third or fourth generation progestin may be helpful.
- 3. Antibiotics:** Oral antibiotics are also effective for moderate to severe inflammatory acne, or for truncal location of lesions. Oral Isotretinoin is the only agent that has demonstrated maximum clinical effectiveness for all forms of acne. It is currently reserved for of severe, nodular acne, in cases scarring, and for milder forms resistant to other treatments

Female pattern hair loss

The mainstay first-line treatment of FPHL is 2% topical minoxidil. The use of 1 ml of minoxidil topically to the scalp skin and hair twice a day is recommended for FPHL. Treatment efficacy should be re-evaluated after 6 months; and, patients should be cautioned against possible increased shedding during the first two month of the therapy.

Follow Up

Before initiation of any medical therapy, expectation of treatment should be discussed with the patient. Managing the symptoms of hyperandrogenism may be a lifelong process. Patients should be assessed at routine intervals (every 3-6 months) for adverse effects and response to treatment

until their condition is stable; they then should be monitored annually. With combination therapy, often antiandrogens can be discontinued or tapered over time, with continuation of oral contraception as monotherapy. Monitoring serum androgens is not recommended. Although data are unclear, consider monitoring potassium levels if patients taking spironolactone have medical comorbidities that affect renal function. Management should be individualized based on spironolactone dose and other comorbidities.

Conclusion

Symptoms of androgen excess are quite common among adolescents and can have a substantial effect on self-esteem and emotional well-being. Among adolescents presenting with these symptoms, it is a challenge to distinguish physiologic changes of puberty from PCOS. Often, a longitudinal assessment of a patient's symptoms, examination findings, and laboratory values are required before a health care provider can distinguish pubertal changes from PCOS. Adolescents with hirsutism or acne can be treated with a goal of symptom control before assignment of a final diagnosis.

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Oral GnRH Antagonist: The New Kid on the Block - What You Can and Cannot Do?



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Introduction

Gonadotropin-releasing hormone (GnRH) plays a central role in the regulation of the hypothalamic–pituitary–gonadal (HPG) axis, controlling secretion of follicle stimulating hormone (FSH) and luteinizing hormone (LH), which in turn regulate ovarian folliculogenesis and steroidogenesis [1]. The advent of GnRH analogues has transformed reproductive medicine over the past three decades. Initially, long-acting GnRH agonists were utilized to suppress premature LH surges in in-vitro fertilization (IVF) cycles, providing a more controlled environment for follicular development [2]. Subsequently, GnRH antagonists were introduced, offering more immediate and reversible suppression without the flare-up effect associated with agonists [3].

Oral gonadotropin-releasing hormone (GnRH) antagonists represent a new treatment option for the treatment of ovarian hormone-dependent diseases in women, including endometriosis and uterine fibroids. Both injectable and oral GnRH antagonists competitively inhibit GnRH receptors in the pituitary gland and lead to a rapid and dose-dependent reduction in circulating gonadotropins and ovarian sex hormones, including estradiol (E2) [4]. Therefore, oral GnRH antagonists provide a potential for adjusting the dose to balance efficacy and safety, which cannot be achieved with depot GnRH agonists and has not been clinically implemented with injectable GnRH antagonists [5].

Elagolix is the first oral uracil derivative nonpeptide GnRH antagonist that have been approved by the US Food and Drug Administration for the management of endometriosis (trade name Orilissa, AbbVie Inc., North Chicago, IL) and heavy menstrual bleeding (HMB) associated with uterine fibroids in combination with hormonal addback therapy (trade name Oriannh, AbbVie Inc., North Chicago, IL). The cloning of the human GnRH receptor and its characterization was a starting point for drug discovery of small molecules that bind to this receptor using high-throughput screening [5]. A focused drug discovery program of oral GnRH antagonists at Neurocrine Biosciences (San Diego, CA) led to the discovery of several lead compounds, including elagolix (Fig. 1), which was selected for clinical development.^{6,7}

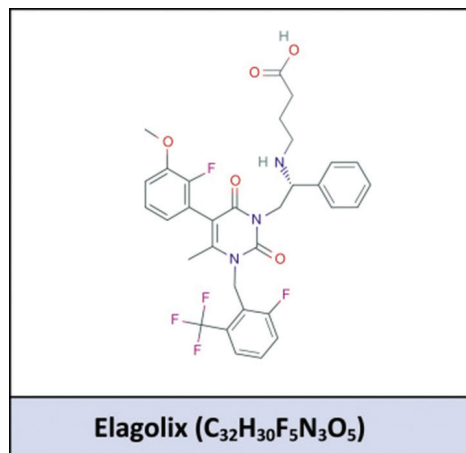


FIG 1. Elagolix has molecular formula of C₃₂H₃₀F₅N₃O₅ and molecular weight of 631.6 g/mol. Elagolix sodium is a non-peptide, amorphous solid orally bioavailable small molecule, that is freely soluble in water. Elagolix at 150 or 200 mg dose, is highly soluble throughout the physiological pH range, and exhibits high aqueous solubility (approximately 1 mg/mL).

Mechanism of Actions

- GnRH Antagonist binds competitively to the GnRH receptor in the pituitary gland & blocks endogenous GnRH signaling
- Rapid suppression FSH & LH
- Gonadotrophin suppression leads to dose-dependent decrease in serum E2 concentration
- Hypoestrogenic state - manages the endometriotic lesions- pain relief.

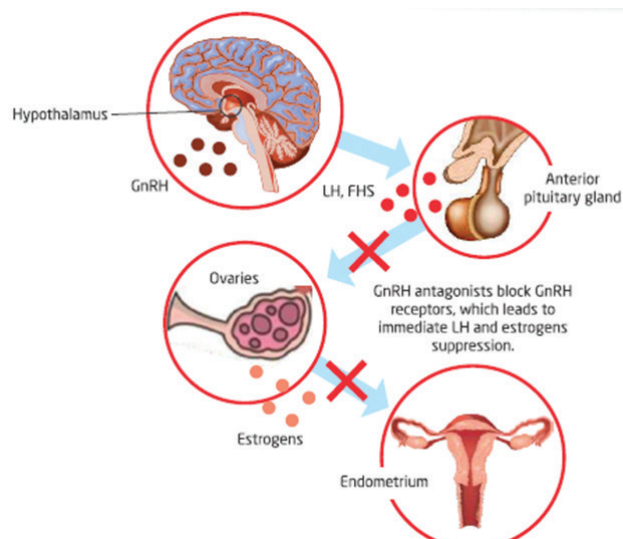


FIG 2. MECHANISM OF ACTION OF GnRH ANTAGONIST

Pharmacodynamics and Pharmacokinetics

The two best-studied oral antagonists are elagolix and relugolix. Elagolix is rapidly absorbed through the gastrointestinal tract following oral administration, reaching its peak plasma concentrations in a dose-dependent manner within 30–60 minutes after an oral dose. Plasma half-life of elagolix varies from 4 to 6 hours [8]. The first human study evaluating the effects of elagolix was published in 2009. It was a randomized, double-blind, placebo-controlled study on 55 healthy premenopausal women, 98 and it reported elagolix's effectiveness in suppression of gonadotropins and oestradiol. A single dose of elagolix between 25 and 400 mg was able to suppress LH levels to 22–35% of

pre dose baseline by 4 hours after administration, with a return to basal levels within 24 hours. A similar pharmacodynamics was observed regard to FSH. Moreover, elagolix administration at 50, 200 and 400 mg resulted in suppression of serum E2 levels to 42–65% of baseline values at 24 hours, with return to baseline in 48 hours. It is mainly metabolized mainly in the liver (CYP 3A) & 90% excreted in feces [8]. Relugolix is rapidly absorbed through the gastrointestinal tract. At a single 40 mg oral dose before breakfast, it reaches a maximum blood concentration after 1.5–2 hours and has a plasma half-life of 45 hours [9]. Linzagolix has a steady pharmacokinetic profile with little variability, due to its high bioavailability and low volume of distribution, so that it remains in the blood rather than in fatty tissues. It has a plasma half-life of 14–15 hours, that allows once daily administration, optimizing patient compliance [10].

TRIALS OF ELAGOLIX

Endometriosis trials

1. Elaris Endometriosis I (EM-I) and II (EM-II)

- Large phase III, randomized, placebo-controlled trials.
- Enrolled premenopausal women with moderate-to-severe endometriosis-associated pain.
- Compared elagolix 150 mg once daily and 200 mg twice daily vs placebo for 6 months.
- Outcomes: Both doses significantly reduced dysmenorrhea and non-menstrual pelvic pain compared to placebo.
- Side effects: Hypoestrogenic symptoms (hot flashes, bone mineral density loss) [11].

2. Long-term Extension Studies (EM-III and EM-IV)

- Evaluated safety/efficacy up to 12 months.
- Showed sustained pain reduction, but with progressive bone mineral density decline in higher dose groups [12]

Table 1: Summary of famous trials of elagolix

Trial (Name/Phase)	Population	Intervention	Comparator	Key Outcomes	Safety Findings
EM-I & EM-II (Phase III, Endometriosis)	Women with moderate-severe endometriosis-associated pain (N≈1700)	Elagolix 150 mg OD, 200 mg BD (6 m)	Placebo	Significant reduction in dysmenorrhea and non-menstrual pelvic pain vs placebo	Hot flashes, headache, bone mineral density (BMD) loss (dose-dependent)

EM-III & EM-IV (Extension, Endometriosis)	Women completing EM-I/II	Continued Elagolix up to 12 m	—	Sustained pain reduction	Progressive BMD decline at high dose, long-term safety concerns
UF-I & UF-II (Phase III, Uterine Fibroids)	Premenopausal women with fibroid-related heavy menstrual bleeding (N≈800)	Elagolix ± add-back (estradiol 1 mg + norethindrone acetate 0.5 mg) for 6 mo	Placebo	≥50% reduction in menstrual blood loss achieved significantly more often with Elagolix + add-back	Add-back reduced vasomotor symptoms and bone loss
UF-III & UF-IV (Extension, Uterine Fibroids)	Women from UF-I/II	Elagolix + add-back up to 12 mo	—	Sustained reduction in menstrual blood loss, improved anemia	Add-back maintained BMD, improved tolerability

Uterine Fibroid Trials

1. Elaris Uterine Fibroids I (UF-I) and II (UF-II)

- Phase III, double-blind, randomized, placebo-controlled trials.
- Evaluated elagolix with add-back therapy (estradiol + norethindrone acetate) vs placebo for 6 months.
- Primary endpoint: Proportion of women achieving ≥50% reduction in menstrual blood loss.
- Results: Elagolix + add-back significantly reduced heavy menstrual bleeding compared to placebo.
- Safety: Add-back therapy mitigated bone loss and vasomotor symptoms[13].

2. Long-term Extension Trials (UF-III, UF-IV)

- Up to 12 months of treatment.
- Confirmed sustained efficacy with add-back therapy and manageable safety profile[14].

Key milestones in the journey of elagolix

On 23rd July 2018, the US FDA approved **elagolix** for the management of moderate to severe pain associated with endometriosis. This was a result of the successful outcome of Two PHASE III clinical trials.

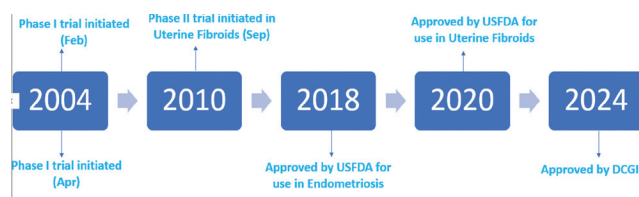


Figure 3: Key Milestones In Elagolix

Clinical Applications: What You Can Do?

1. Controlled Ovarian Stimulation in ART

The first study investigating the use of oral GnRH antagonists in IVF was a cross-sectional retrospective study by Nakao et al. [15]. A number of 230 IVF cycles performed with a mild ovarian stimulation were evaluated. The study group using relugolix 40 mg daily to suppress ovulation was compared to a control group using a conventional injective GnRH antagonist. The study reported a very low percentage of spontaneous ovulation in both groups (1.9% and 2.4%, respectively, $p = 0.84$). Moreover, there were not significant differences between groups regarding the number of retrieved oocytes, the fertilization rate, the blastocyst development rate, the clinical pregnancy rate after embryo transfer with either cleavage or blastocyst stage embryos[15]. The oral route significantly reduces injection burden, improving patient satisfaction. For many women undergoing multiple cycles of IVF, switching from daily injections to oral medication could reduce anxiety and improve treatment adherence.

2. Management of Endometriosis

Endometriosis is a chronic estrogen-dependent condition characterized by the ectopic implantation of endometrial glands & stroma outside of the uterine cavity. Endometriosis affects 10% (190 million) of reproductive age women and girls globally [16]. Asian women were reported to have higher prevalence of endometriosis and higher frequency of moderate-to-severe endometriosis.

Optimal goal of medical therapy

Estrogen Threshold Hypothesis

- Ideal treatment : lower E2 levels to treat symptoms, while maintaining sufficient levels

to reduce side effects

2. Partial suppression E2 within 30-50 pg/ml-optimal to maintain its efficacy, tolerance and safety.

E2<20pg/ml – causes lesion to regress with substantial bone loss.

E2 >60pg/ml – supports growth of endometriotic lesion [17]

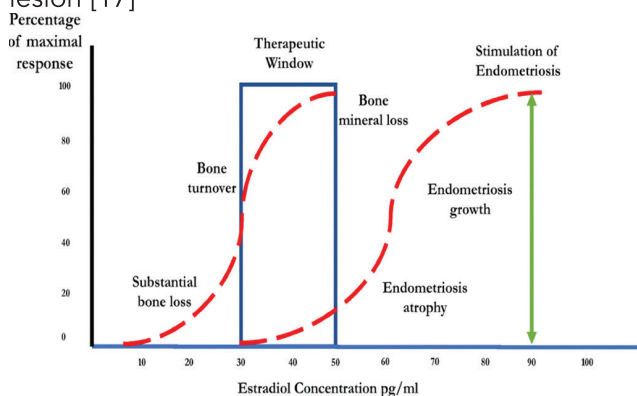


Figure 4: Estrogen Threshold Hypothesis

Clinical guide to the treatment of endometriosis with elagolix

- Dose dependent suppression of FSH & LH within 4-6 hours after single dose
- 2 dosage regimen allows individualization of treatment : Clinical presentation, response & tolerability.

Table 2: Guide To The Treatment Of Endometriosis With Elagolix

Drug	Dose Regimen	Median Estradiol Concentration
Elagolix	150 mg OD, Orally	42 pg/mL
Elagolix	200 mg BD, Orally	12 pg/mL

Clinical evidence has shown that elagolix at both approved doses (150mg once daily and 200mg twice daily) is effective for reducing symptoms of pelvic pain (dysmenorrhea, nonmenstrual pelvic pain, and dyspareunia), improving quality of life, and decreasing use of rescue analgesics (nonsteroidal anti-inflammatory drugs and/or opioids). The availability of two dosing options allows for individualization of treatment based on baseline clinical factors and response to therapy. Unlike injectables, oral formulations allow titration of dose to achieve partial suppression, minimizing hypoestrogenic side effects such as bone mineral density loss and vasomotor symptoms [18].

3. Uterine Fibroids

Uterine Fibroids are the most common benign tumor in reproductive age women worldwide, with financial burden of hundreds of billions of dollars annually including direct cost of hospital admission and medical management as well as indirect cost of loss of wages and productivity loss. Unfortunately, there is limitation in available long-term treatment options. Thus, there is a large unmet need in the UF space for noninvasive therapeutics. Elagolix is an oral GnRH antagonist that suppresses steroidal hormones production in a dose-dependent manner. Elagolix with add-back therapy is the first oral FDA approved drug for management of UF associated HMB up to 24 months due to the risk of continued bone loss[19].

Limitations: What You Cannot Do (Yet)?

1. Universal Application in All ART Patients

While promising, oral antagonists are not yet validated for all categories of IVF patients. Their efficacy in poor responders, women with polycystic ovary syndrome (PCOS), or those at high risk of ovarian hyperstimulation syndrome (OHSS) is less clear [20]. Until more data are available, clinicians must be cautious in extrapolating their use universally.

2. Substitute for Injectable Antagonists in All Settings

Despite their convenience, oral antagonists cannot yet fully replace injectable antagonists in ART. Large randomized controlled trials (RCTs) comparing pregnancy rates, live birth rates, and safety outcomes between oral and injectable antagonists are still limited [21].

3. Long-Term Safety Concerns

Long-term safety data remain sparse. While bone density loss appears reversible with add-back therapy, the implications of chronic suppression, especially in younger women desiring fertility preservation, are unknown. Similarly, potential cardiovascular or metabolic impacts of prolonged hypoestrogenism warrant further investigation.

4. Accessibility and Cost

High cost is a significant barrier to widespread adoption, particularly in low- and middle-income countries where IVF treatment is already financially burdensome. In addition, regulatory approval varies geographically, limiting access in some regions.

5. Patient Adherence in Real-World Settings

Although oral therapy improves convenience, adherence is not guaranteed. The shorter half-life of elagolix necessitates strict twice-daily dosing, and missed doses could compromise efficacy [22]. Injectable formulations, in contrast, provide more reliable suppression once administered.

Future Directions and Research Gaps

The future of oral GnRH antagonists appears promising but requires further evidence. Ongoing research is exploring their role in other gynecological conditions like adenomyosis, AUB and their use in personalised medicine approaches. Further head-to-head trials are required to compare oral versus injectable antagonists for live birth rates, OHSS prevention, and patient satisfaction, and to address the concerns regarding long term safety. Ultimately, oral antagonists may complement, rather than replace, existing injectable options, providing clinicians with greater flexibility to individualize treatment.

Conclusion

Oral GnRH antagonists represent an exciting innovation in reproductive medicine, bridging pharmacological efficacy with improved patient convenience. They offer significant advantages in ART protocols, endometriosis, fibroids, and menstrual suppression, while enhancing patient compliance. However, they remain the “new kid on the block,” with important caveats regarding universal applicability, long-term safety, accessibility, and cost. At present, they should be viewed as valuable additions to the therapeutic armamentarium, rather than wholesale replacements for injectable analogues. Future research will determine whether they become mainstream in fertility practice or remain niche options. For clinicians, the key lies in balancing enthusiasm for novelty with evidence-based caution, ensuring that patient outcomes remain the central focus.

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Interpreting Abnormal Semen Analysis and Next Steps



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Introduction

Infertility is defined as the inability of a couple to conceive even after 1 year of unprotected, frequent sexual intercourse. Male factor is the sole cause in about 20-30% of cases and is a contributing factor in another 20% to 40% of cases. This means a male factor is involved in about 50% of all infertility cases.¹

Semen analysis remains the mainstay for evaluating the male partner in infertility work up. It reflects the ejaculatory function, testicular spermatogenic capacity, patency of the male reproductive tract and the functioning of accessory glands. Despite its clinical utility; semen analysis has its limitations: Neither is an abnormal result diagnostic of permanent infertility, nor is a normal test considered an absolute proof of fertility.

An abnormal semen analysis can be a source of significant anxiety for patients, and a clear, empathetic explanation of the findings and the path forward is essential. This review aims to demystify abnormal results, provide a structured approach to interpretation, and outline a clear, evidence-based plan for the next steps.

Normal Semen Parameters

The World Health Organization (WHO) released the 6th edition of its laboratory manual for human semen analysis in 2021, providing updated lower reference limits derived from fertile men.²

Here is a table outlining the semen parameters and their reference values (6th edition):

Table 1: Semen Analysis Parameters (WHO 2021)²

Semen parameter	One sided lower reference limit (5th centile with 95% confidence intervals {CI})
Semen volume	1.4 ml (1.3 – 1.5 ml)
Sperm concentration	16 million per ml (15- 18 million/ ml)
Total sperm number	39 million per ejaculate (35- 40 million per ejaculate)

Total motility(PR+NP, %)	42 %(40-43%)
Progressive motility(PR)	30% (29-31%)
Non Progressive motility(NP)	1%
Immotile spermatozoa (IM)	20%
Normal morphology	4% (3.9- 4%)
Vitality	54% live (50-56%)
pH	>7.2
Pus cells	< 1 million per ml

Normozoospermia : Normal semen parameters meeting the above mentioned criteria indicating optimal fertility potential.

Interpreting abnormal semen analysis(SA)

Results of SA are of greatest clinical significance when multiple abnormalities are present.² While certain abnormalities like

azoospermia, some types of teratozoospermia (e.g., complete globozoospermia), necrozoospermia or complete asthenozoospermia are diagnostic of infertility², none of the other individual parameter derangements indicate absolute infertility. The odds ratio for infertility increases as the number of abnormal parameters increases.³

Table 2: Terminology Based on the Abnormality in Semen Parameter

Aspermia	Complete absence of semen in ejaculate
Oligozoospermia	Low sperm concentration in the semen
Azoospermia	Absence of spermatozoa in the semen, either due to blockage in the reproductive tract (obstructive azoospermia) or dysfunctional spermatogenesis (non-obstructive azoospermia).
Asthenozoospermia	Reduced sperm motility, sluggish or abnormal movement is seen in a significant proportion of sperms
Teratozoospermia	Abnormal sperm morphology, a high percentage of spermatozoa have morphological defects
Retrograde Ejaculation	Semen flows backward into the bladder instead of exiting through the urethra during ejaculation.
Leukocytospermia	>1 million leukocytes per ml (Excessive leukocytes in semen)

Azoospermia: Absence of spermatozoa in the semen after examination of the centrifuged pellet, on 2 occasions at least 1-2 weeks apart⁴

What Next After an Abnormal Semen Analysis (Sa):

STEP 1: REPEAT SA

Considering the high degree of variability in semen analyses in the same individual, abnormality detected in SA should be confirmed by a repeat test.

Repeat SA is recommended 2-3 months after the initial one, to account for the full spermatogenesis cycle (approximately 72 days).⁵ Exceptions include cases with absent sperms or very low sperm count, where earlier testing is warranted.

Whenever a semen sample is collected, adherence to pre- test instructions must be ensured, including 2- 7 days of prior sexual abstinence², collection of sample by masturbation into a wide mouthed container; making sure there is no loss of semen during collection. Ideally, the sample should be collected close to the lab.

If sample is collected away from laboratory, transport should be done at 20-37 deg C temperature, by keeping the sample close to the body ; sample should reach lab ideally within 30 minutes; and not later than 50 minutes of sample collection.

Although masturbation is the preferred method of ejaculate collection; special condoms for fertility investigation may be used. Condoms are not preferred as there is risk of incomplete sample collection and contamination by penile skin and vaginal fluid. Coitus interruptus and contraceptive/ latex condoms are not recommended as they contain spermicidal agents and agents which interfere with sperm motility.

Semen examination should be commenced within 30 minutes of collection; Latest within 60 minutes(2).

STEP 2: HISTORY AND PHYSICAL EXAMINATION

Detailed history should encompass:

1. Sexual developmental history, including testicular descent, pubertal development, loss of body hair, or decrease in shaving frequency.
2. History of major head trauma, pituitary tumour, surgery, or irradiation that could result in hypogonadotropic hypogonadism.
3. Infections such as mumps orchitis, recurrent sinopulmonary symptoms, sexually transmitted infections, and genitourinary tract infections (eg- prostatitis).
4. Surgery or trauma in the pelvic or genital area.
5. Drugs and adverse environmental exposures such as marijuana, opioids, radiotherapy, corticosteroids, chemotherapy, drugs that cause hyperprolactinemia, and exposure to toxic chemicals (eg, pesticides).
6. Sexual history, including libido, frequency of intercourse.
7. Lifestyle factors: high heat exposure (hot tubs, saunas), prolonged cycling, Smoking, alcohol consumption, drug use (recreational and anabolic steroids), occupation, excessive exercise
8. Chronic medical illness like diabetes mellitus,

thyroid disorders

EXAMINATION.

The examination of the man should include the following components:

- General physical examination: BMI, gynecomastia, secondary sexual characters, virilization, overt signs of thyroid dysfunction
- Skin – Hyperpigmentation may indicate iron overload. Men with Cushing syndrome may have thin skin, ecchymoses, and/or broad purple striae. Loss of pubic, axillary, and facial hair, decreased oiliness of the skin, and fine facial wrinkling suggest long standing testosterone deficiency.
- External genitalia – :
 1. Incomplete sexual development: Small testes and other findings of incomplete pubertal development (Tanner stage less than 5).
 2. Diseases that affect sperm maturation and transport: detected by examination of the scrotum for absence of the vasa, epididymal thickening, and large varicoceles.
 3. Testicular volume or size: Subnormal testicular volumes correlate with decreased sperm production and sperm concentrations in the ejaculate. In an adult man, a testicular volume less than 15 cc or a testicular length less than 3.6 cm is considered small (measured by Prader orchidometer or calipers). FSH > 7.6 IU/L and testis longitudinal axis < 4.6 cm indicate an 89% likelihood of spermatogenic dysfunction as the etiology.⁶

3) STEP 3: FURTHER TESTING

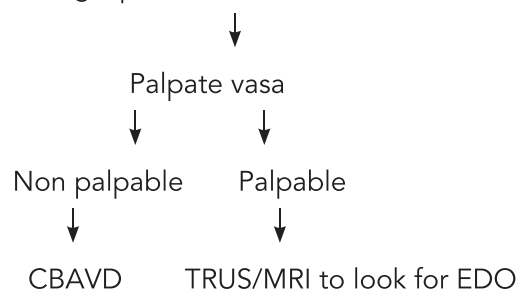
The abnormality detected SA guides towards further evaluation/testing to identify the cause, and offer targeted treatment.

A) LOW SEMEN VOLUME

- Ensure that abstinence interval was optimum (Short abstinence interval can lead to low volume semen)
- Rule out spillage of semen during collection.
- Evaluate for retrograde ejaculation: a urine specimen is collected immediately after ejaculation. It is then centrifuged and microscopically examined for spermatozoa. The presence of substantial sperm in the post-ejaculatory urine specimen confirms retrograde

ejaculation.⁷

- Low semen volume and low sperm count can occur in men with testosterone deficiency.
- Low volume acidic semen with no sperm or severely low sperm count raises a suspicion of ejaculatory duct obstruction(EDO) or congenital bilateral absence of the vas deferens(CBAVD).
- Transrectal ultrasound (TRUS) or pelvic MRI is recommended in males with acidic, azoospermic semen with volume <1.4mL, with normal serum testosterone (T) and palpable vas deferens- to look for EDO.⁸
- Low volume acidic semen with azoospermia/severe oligospermia



(B) LOW SPERM COUNT

OLIGOSPERMIA AND AZOOSPERMIA: Endocrine testing- FSH and testosterone is recommended (8)

Initial endocrine testing: FSH and fasting total testosterone (8-10 am)

↓

If total testosterone < 300 ng/ml^{8,9}

↓

LH, estradiol and prolactin

Primary infertility with Azoospermia or severe oligozoospermia(sperm concentration < 5 million /ml): karyotype testing is recommended (when FSH is elevated, there is testicular atrophy, or a diagnosis of impaired sperm production.) Klinefelter syndrome is common in these men, and chromosomal translocations occur in up to 15 percent of men with severe oligozoospermia or azoospermia.

Primary infertility and azoospermia or sperm concentration ≤1 million sperm/mL: Y-chromosome microdeletion analysis (when accompanied by elevated FSH, testicular atrophy, or a diagnosis of impaired sperm production.

Vasal agenesis or idiopathic obstructive azoospermia: Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) mutation carrier

testing is recommended.

Scrotal Ultrasound: Indicated for suspected varicocele, testicular atrophy, or obstruction. It can visualize testicular architecture and epididymal cysts.

(C) INCREASED ROUND CELLS

Excess Round cells in semen can be:leucocytes, epithelial cells,immature germ cells (spermatocytes,spermatids).

Increased round cells on semen analysis(>1 million/mL)should trigger further evaluation to differentiate germ cells from white blood cells(WBCs)(8)

Differentiation can be done by o-toluidine test for cellular peroxidase (peroxidase stain)that will not stain leukocytes or, Immunocytochemical staining(using antibodies specific for common leukocyte antigens)which can more precisely identify the WBCs.

In patients with pyospermia(excess WBCs),evaluation and treatment for infection is recommended.This is essential because elevated semen WBCs may secrete cytokines and generate free radicals in the semen(reactive oxygen species) that may be detrimental to sperm function.

(D) POOR MOTILITY — Men with a very high percentage of immotile sperm might still be treatable with intracytoplasmic sperm

injection(ICSI).If very low or no motile sperms are found in semen, a vitality test is done to look for live sperms.

- Hypo osmotic swelling test(HOS test) and
- Dye exclusion test: eosin nigrosin test
 - HOS test procedure :sperms are incubated in a hypo-osmotic solution
 - the tails of viable sperms(with normal membrane function) swell and coil.
 - Dye exclusion test:
 - fresh semen is mixed with supravital dye(eosin Y or trypan blue).
 - Sperms with intact membranes(live sperms) do not take up the stain

(E) ABNORMAL MORPHOLOGY

In cases of severe,monomorphic teratozoospermia, where a high percentage of sperms share a single, specific abnormality (e.g., globozoospermia or macrozoospermia), genetic testing may be done. Key genes identified are AURKC and DPY19L2. Genetic testing can help refine diagnosis and guide treatment, especially in cases where ICSI may have a poor outcome.¹⁰

Morphologically normal sperm can be selected through IMSI(Intracytoplasmic Morphologically Selected Sperm Injection) in ART(Assisted Reproductive Technology).

Table 3: Diagnosis & Management of Male Infertility :

	FSH	LH	Testoster-one	Testicular Volume	Treatment
Pretesticular	Low	Low	Low	Low	Gonadotropin therapy: HCG alone or HCG with HMG or FSH
Testicular	HIGH (>7.6 IU/L)	HIGH or normal	LOW or normal	LOW/ NORMAL	1) Where applicable: remove drugs/toxins, varicocele repair 2) Surgical sperm retrieval- IVF/ICSI OR 2) donor sperm IUI OR 3) adoption
Post Testicular (Obstructive)	Normal	Normal	Normal	NORMAL. EPIDIDYMIS may be dilated or indurated.	Surgical correction of block (Vasovasostomy, TURED) OR Surgical sperm retrieval and ICSI/IVF

HCG: Human chorionic gonadotropin; FSH: Follicular stimulating hormone; HMG: Human menopausal gonadotropin
TURED: Transurethral resection of ejaculatory ducts; IVF: Invitro fertilization; ICSI: Intracytoplasmic sperm injection
IUI: Intrauterine insemination

Treatment: Individualized, depending on the cause of infertility.

A. Lifestyle modification: Men are advised to quit smoking, reduce alcohol intake, avoid toxins, heat exposure which can interfere with spermatogenesis. They are counselled to achieve and maintain a healthy weight; as overweight and obese men may have higher estradiol levels due to peripheral aromatization, leading to a negative feedback effect on hypothalamic-pituitary-gonadal axis and hence a negative impact on spermatogenesis.¹¹

B. Medical treatment:

(i) Gonadotropins :

- Hypogonadotropic hypogonadism(HH)-Gonadotropins are therapeutic in these cases. Treatment begins with 1000–2500 IU of HCG twice a week for 8–12 weeks.¹². Administration of FSH 150-300 IU two to three times a week for upto 18 months is required for patients with congenital HH or adult-onset HH who lack adequate concentrations of endogenous FSH¹³. In patients with HH, evaluation to determine the etiology and targeted treatment is required.⁸
- Idiopathic infertility:FSH analogue may be used with the aim of improving sperm concentration, pregnancy rate, and live birth rate.⁸

(ii) Selective estrogen receptor modulators(SERM):Although there is limited benefit of SERMs in idiopathic male infertility compared to ART(8);there is some evidence of improvement in sperm concentration with treatment.¹⁴

(iii) Aromatase inhibitors (Letrozole/ anastrozole):Use of these drugs significantly improve seminal and hormonal parameters in obese men with low Testosterone/Estradiol ratio(<10), though the effect on semen parameters was comparable to that seen with SERM or HCG.¹⁵

Although,SERMs, AI, HCG or a combination of these may be useful in males with low testosterone(8); further well designed RCTs are needed to further establish the role of aromatase inhibitors and SERMs in male infertility.

(iv) Antioxidants:Antioxidants have been used empirically in males with abnormal semen

parameters, on the pretext that oxidative stress can damage sperms and lead to increased sperm DNA fragmentation. Recent Cochrane review suggests that evidence is inconclusive about benefit of antioxidants in subfertile males. There is very low-certainty evidence suggesting that antioxidant supplementation may improve live birth rates(16). ASRM guidelines⁸ also infer that the benefits of supplements(e.g.,antioxidants,vitamins)are of questionable clinical utility in treating male infertility.

C. Surgical varicocelectomy is recommended for males attempting to conceive and who have palpable varicocele(s),infertility and abnormal semen parameters, except for azoospermic males.Varicocelectomy is not recommended for males with non-palpable varicoceles, detected by imaging.Varicocele with azoospermia:recommend surgical sperm retrieval and ART; not varicocelectomy.

D. IUI(Intra uterine insemination):Minimally invasive treatment involving the deposition of washed concentrated highly motile sperms in the uterus around the time of ovulation. It can be used in mild to moderate male factor infertility. Evidence indicates that a post-wash total motile sperm count (TMSC) of 5 to 10 million motile sperms is the optimal range for IUI success. Success rates increase as the TMSC rises.¹⁷ Best results are observed with a TMSC> 10 million. The minimum threshold for an IUI cycle is a post-wash TMSC of 1 million motile sperm. However, pregnancy rates at this level are very low (often less than 5%) and IVF is a preferred treatment. Donor sperm IUI may be offered in patients with azoospermia who are not amenable to or not willing for sperm retrieval and IVF.

E. Sperm retrieval and ART:

In cases of severe oligospermia,asthenospermia and azoospermia,IVF with ICSI are the preferred treatment. In cases of azoospermia, surgical sperm retrieval followed by ICSI is done with fresh or frozen sperms.

In men with non-obstructive azoospermia, microdissection testicular sperm extraction (micro-TESE) is recommended for sperm retrieval.⁸ In obstructive azoospermia, surgical sperm retrieval is done from either the testis or the epididymis.

In cases of aspermia, clinicians may perform surgical sperm extraction or induced ejaculation (sympathomimetics, vibratory stimulation or electroejaculation).

(iii) Surgical correction of obstruction:

- After vasectomy: Surgical reconstruction, surgical sperm retrieval, or both reconstruction and simultaneous sperm retrieval for cryopreservation are viable options.
- Vasal or epididymal obstructive azoospermia: microsurgical reconstruction may be successful
- Ejaculatory duct obstruction: TURED and/or surgical sperm extraction can be offered.

Emerging Concepts

APHRODITE classification: Addressing male patients with Hypogonadism and/or infertility owing to altered, Idiopathic Testicular function – stratifies eligible patients into five different subgroups. For each subgroup, specific suggestions are given for medical treatment using hormonal therapy to improve sperm quantity and/or quality.¹⁸

Conclusion

Abnormal semen analysis is a frequent yet complex finding in infertility evaluation. Interpretation requires repeat testing, clinical correlation, and structured investigations. Management is individualized, ranging from lifestyle interventions to ART. The ultimate goal is not just interpreting numbers but supporting couples in achieving parenthood with compassion and evidence-based strategies.

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JOURNAL SCAN



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Therapeutic management in women with a diminished ovarian reserve: a systematic review and meta-analysis of randomized controlled trials

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2024 Sep 26

This systematic review and meta-analysis by Conforti et al. (2025) assessed the effectiveness of various therapeutic strategies in women with diminished ovarian reserve (DOR), a group that typically exhibits poor response to ovarian stimulation and reduced live birth rates. The authors included 38 randomized controlled trials published up to June 2024, encompassing several adjuvant interventions and stimulation protocols. Women were defined as having DOR using POSEIDON criteria or biomarkers such as low antral follicle count (AFC) or anti-Müllerian hormone (AMH). The primary outcome was live birth rate or ongoing pregnancy rate (when live birth was not available), while secondary outcomes included the number of oocytes retrieved, metaphase II (MII) oocytes, clinical pregnancy rate, and miscarriage.

The most notable finding was that testosterone supplementation significantly improved live birth rate compared with controls (odds ratio [OR] 2.19, 95% confidence interval [CI] 1.11–4.32; 4 RCTs, 368 patients). In addition, testosterone pretreatment increased the number of retrieved oocytes (weighted mean difference [WMD] 0.88, 95% CI 0.03–1.72). Dehydroepiandrosterone (DHEA) also showed a modest benefit, with an increase in oocyte yield (WMD 0.60, 95% CI 0.07–1.13; 4 RCTs, 418 patients). Similarly, the delayed-start antagonist protocol resulted in significantly more oocytes retrieved compared to conventional

antagonist regimens (WMD 1.32, 95% CI 0.74–1.89; 3 RCTs, 398 patients). In contrast, low-dose gonadotropin protocols produced fewer oocytes than high-dose regimens (WMD –1.57, 95% CI –2.12 to –1.17; 2 RCTs, 905 patients), suggesting that dose reduction is not advantageous in this population.

Other tested interventions, including letrozole, clomiphene citrate, growth hormone, luteal-phase stimulation, dual stimulation, luteinizing hormone supplementation, estradiol pretreatment, and corifollitropin alfa, did not demonstrate consistent improvements in live birth, clinical pregnancy, or oocyte outcomes.

In conclusion, this meta-analysis highlights testosterone supplementation as the most promising intervention for women with DOR, with evidence for improved live birth and oocyte yield. However, the overall number of trials and sample sizes remain limited, and protocol heterogeneity was considerable. The authors emphasize the need for larger, well-designed RCTs to confirm the benefits and establish standardized treatment strategies for this challenging patient group.

Livebirth rates are influenced by an interaction between male and female partners' age: analysis of 59 951 fresh IVF/ICSI cycles with and without male infertility

Hum Reprod.2024 Nov 1;39(11):2491-2500. doi: 10.1093/humrep/deae198

In a comprehensive retrospective analysis of 59,951 fresh IVF/ICSI cycles from 2017 to 2018 in the UK, Datta et al. investigated how male partner age interacts with female partner age to influence live birth rates (LBRs) in assisted reproduction. The cohort included 27,226 IVF

cycles and 32,725 ICSI cycles, excluding cases of oocyte donation, PGT, endometriosis, or ovulatory disorders. Women were stratified into age groups (< 35, 35–39, 40–42, 43–44 years), and men into multiple age bands (< 35 as reference, 35–37, 38–39, 40–42, 43–44, 45–50, 51–55, > 55).

The authors found that across male age groups, there was no statistically significant difference in LBR per oocyte retrieval (or per ET) when the female partner was < 35 or ≥ 40 years old — in both IVF and ICSI settings, irrespective of male factor infertility. However, in women aged 35–39 years undergoing IVF, increasing male age ≥ 40 was associated with a sharp decline in LBR: from 27.0% in male < 35 years to 22.9% ($P = 0.002$) in 40–44 years, 22.0% ($P = 0.006$) in 45–50 years, and 18.8% ($P = 0.004$) in > 50 years. Similar declines were noted when excluding male infertility: from 27.6% in reference male age to 23.5% ($P = 0.002$) in

40–44 and 22.2% ($P = 0.002$) in older male groups. Notably, no such male age effect on LBR was seen when fertilization was via ICSI, in any female age group, regardless of inclusion of male-factor cycles.

Adjusting for confounders (female and male age, previous cycles, prior live birth, insemination method, embryo number and stage), the adverse effect of male age remained significant only in the subgroup of women aged 35–39 undergoing IVF. Miscarriage rates per single embryo transfer showed a non-significant upward trend when male partners were > 55 years, particularly in female partners < 40 years; a statistically significant increase was found only in the IVF subgroup of women aged 40–44 and men > 55 ($P = 0.02$). The authors conclude that male partner age exerts a deleterious influence on live birth only in mid-aged female partners (35–39 years) and only when using conventional IVF, suggesting that ICSI may mitigate the impact of paternal age in this group.

QUIZ TIME

Gynaecological Endoscopy



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Q1.: Which hormone is primarily responsible for the mid-cycle LH surge leading to ovulation?

- a) FSH b) Progesterone c) Estradiol d) Inhibin B

Q2.: The two-cell, two-gonadotropin theory of ovarian steroidogenesis states that:

- a) Granulosa cells produce estrogen independently
b) Theca cells produce estrogen directly from cholesterol
c) Theca cells produce androgens which are aromatized to estrogens in granulosa cells
d) Both theca and granulosa cells can aromatize androgens to estrogens

Q3.: Which of the following hormones shows a pulsatile release that is crucial for normal reproductive function?

- a) LH b) FSH c) GnRH d) Estradiol

Q4.: Which enzyme is deficient in congenital adrenal hyperplasia (CAH) leading to salt-wasting and virilization?

- a) 11 β -hydroxylase b) 17 α -hydroxylase
c) 21-hydroxylase d) Aromatase

Q5. : Kisspeptin plays a crucial role in reproduction by:

- a) Directly stimulating FSH and LH release
b) Suppressing GnRH secretion
c) Activating GnRH neurons in the hypothalamus
d) Inhibiting aromatase activity

Q6.: Which of the following is NOT a function of progesterone in the luteal phase?

- a) Endometrial secretory transformation
b) Decreasing uterine contractility
c) Stimulating cervical mucus production to be thin and watery
d) Supporting early pregnancy

Q7.: Leptin's primary role in reproduction is:

- a) Direct stimulation of gonadal steroidogenesis
b) Acting as a permissive signal for GnRH release
c) Inhibiting LH secretion
d) Inducing ovulation directly

Q8.: Which of the following conditions is characterized by high LH:FSH ratio?

- a) Hypogonadotropic hypogonadism b) Polycystic Ovary Syndrome (PCOS)
c) Premature Ovarian Insufficiency d) Kallmann Syndrome

Q9.: In male reproductive endocrinology, testosterone is mainly converted to dihydrotestosterone (DHT) by:

- a) Aromatase b) 5 α -reductase c) 17 β -HSD d) 11 β -HSD

Q10. : During menopause, which hormone remains relatively stable compared to others?

- a) Estradiol b) Progesterone
c) AMH d) Androgens (testosterone)

Answer : 1 - c) Estradiol; 2 - c) Theca cells produce androgens which are aromatized to estrogens in granulosa cells.; 3-c) GnRH; 4 - c) 21-hydroxylase; 5 - c) Activating GnRH neurons in the hypothalamus; 6-c) Stimulating cervical mucus production to be thin and watery; 7 - b) Acting as a permissive signal for GnRH release; 8 - b) Polycystic Ovary Syndrome (PCOS); 9 - b) 5 α -reductase; 10 - d) Androgens (testosterone).

Activities Under NARCHI June 2025

CAMP HELD ON 28th June 2025

"Public Awareness & Camp for HPV Vaccination" on 28th June 2025 under the aegis of NARCHI Delhi Chapter organized by Institute of Obstetrics & Gynaecology, Sir Ganga Ram Hospital.

Free HPV vaccines were given to more than 220 girls less than 26 yrs of age.

We were blessed by our chief guests Dr. Jayashree Sood, Guest of Honor Dr. Kanwal Gujral, Dr. Geeta Mediratta, Dr. Mala Srivastava, Dr. Chandra Mansukhani & Dr. Kanika Jain. About 200 delegates participated in this camp. This endeavor was highly appreciated and requests came for more such activities in future.



Activities Under NARCHI August 2025



The 31st Annual conference of NARCHI Delhi Chapter was organized by Sir Ganga Ram hospital from 8th Aug to 10th Aug 2025 at India Habitat Centre. This conference was a unique clinical and scientific event that emphasized on multidisciplinary collaboration. The theme of the conference was "Plan Promote Propagate Women's Health".

About sixteen workshops were organized starts from 4th Aug upto 11th Aug, 2025. With this conference we were having sixteen workshops starting from "Theme: Navigating Fetal Anomalies – From Antenatal Diagnosis to Fetal Therapy", "Workshop for Asha Workers", "Empowering Frontline Care: Maternal health Nurses module", "Advance Oncology- Management of Toughest Cases and Recent Updates 2025", "POCT in Critical Care Obstetrics", "Hysteroscopy made easy: a hands-on workshop", "From Screening to Strategy: Preventing Gynecologic Cancers", "Optimizing Intrapartum Surveillance: Principles of physiological interpretation of CTG", "Menopause: Unlocking the potential of the second innings", "Patient Safety", "Promoting Fertility in Endometriosis for Practising Gynaecologist", "Genetic in Obs &

Gynae", "Quality in Maternity Care", "Obstetric Anal Sphincter Injuries Workshop (OASIS)", "Adolescent Health", together with workshop on optimizing surgical outcomes with SNPWT organised by "Smith & Nephew".

The conference had two orations Leelawati & Dr. S.K. Das orations. President Elect Dr. Bhaskar Pal delivered Dr. S. K. Das oration and spoke on "COCP : Tailoring Therapy, Bursting Myths". Past FOGSI President Dr. S. Shantha Kumari delivered Leelawati oration and spoke on "No to Violence Against Women : WHERE ARE WE ??".

There were 104 candidates participated in free paper presentation (22), E Posters (32), Quiz competitions (40) and Slogan Competition (10). Dr. Maria Haroon achieved 1st prize, Dr. Balla Vani received 2nd prize, Dr. Divya Rashmi received 3rd prize in the free paper presentation, Dr. Kareena Rai received 1st prize, Dr. Vidushi Agarwal received 2nd prize and 3rd prize shared by Dr. Sakshi & Dr. Shreya Mahajan in the E poster presentation, Dr. Rishav Dubey received 1st prize, 2nd prize received by Dr. Anu and Dr. Chaiti Saha, 3rd prize received by Dr. Maneesha Verma & Dr. Nikhil Ritolia in Quiz competition. Dr. Maneesha Verma received 1st prize, 2nd prize received by Dr. Neha Pandey, 3rd prize received by Dr. Yogita Chauhan and 4th prize received by Dr. Sangeeta & Dr. Neha in the Slogan Competition.

The delegates thoroughly enjoyed doing the lectures and hands on experience. Overall the conference was very successfully with total 280 registrations.

NARCHI Souvenir were released by Dr Ajay Swaroop, Dr Jayashree Sood & esteemed faculty



NARCHI Inauguration by

Dr Ajay Swaroop, Dr Jayashree Sood & Dr. Manju Puri



Fetal Therapy : Expectations & Preparedness

4th Aug 2025 at Sir Ganga Ram Hospital

Conveners : Dr. Nandita Dimri; Co- conveners : Dr. Nidish Sharma





Asha Workerson 5th Aug 2025 Pre Lunch at Sir Ganga Ram Hospital

Convener : Dr. Shivani Agarwal; Co-convener : Dr. Anita Rajhoria & Dr. Seema Singhal



Nurses Workshop on 5th Aug 2025 Post Lunch at Sir Ganga Ram Hospital

Convener : Dr. Seema Prakash; Co-convener : Dr. Rashmi, Dr. Neha Varun & Dr. Anita Rajhoria



Advance Oncology on 6th Aug 2025 at Sir Ganga Ram Hospital

Dr. Aditya Sarin (Conveners)



HYSTEROSCOPY MADE EASY : A HANDS ON WORKSHOP ON 7TH AUG 2025 AT SIR GANGA RAM HOSPITAL

Conveners : Dr. Kanika Jain; Co- conveners : Dr. Swati Agarwal



POCT in Critical Care Obstetrics 7th Aug 2025 at Safdarjung Hospital

Dr. Jyotsana Suri & Dr. Rekha Bharti (Conveners)

Dr. Sheeba Marwah & Dr. Zeba Khanam (Co-conveners)



FROM SCREENING TO STRATEGY : PREVENTING GYNECOLOGIC CANCERS

7th Aug 2025 at UCMS & GTB Hospital

Dr Rachna Agarwal (Organising chairperson); Dr Bindiya Gupta & Dr Anshuja Singla (conveners)



OASISon 8th Aug 2025 at Sir Ganga Ram Hospital

Conveners : Dr. Geeta Mediratta; Co- conveners : Dr. Sharmistha & Dr. Huma Ali



Patent Safety Workshop on 8th Aug 2025, at Mapple, India Habitat Centre

Conveners : Dr. Poonam Joon; Co- conveners : Dr. Mala Srivastava



Promoting Fertility in Endometriosis for Praticing Gynecologist Pre-Conference Workshop on 8th Aug 2025, at Casuarina, India Habitat Centre

Dr. Shweta Mittal (Conveners); Dr. Neeti Tiwari (Co- conveners)



Menopause Unlocking the Potential of the 2nd Innings Pre – Conference Workshopon 8th Aug 2025, at Gulmohar, India Habitat Centre

Conveners: Dr. Urvashi Miglani, Dr. Harvinder Kaur



Optimizing Intrapartum Surveillance : Principles of Physiological Interpretation of CTG- Pre – Conference Workshopon 8th Aug 2025, at Magnolia, India Habitat Centre

Convener : Dr. Aruna Nigam: Co- Convener : Dr. Sumedha Sharma



ADOLESCENT HEALTH on 11th Aug 2025 at Sir Ganga Ram Hospital

Convener : Dr. Latika Bhalla ; Co- Convener : Dr. Chandra Mansukhani



Two Orations held on on 9th & 10th Aug 2025, at Gulmohar, India Habitat Centre



Dr. S. Shantha Kumari (Leelawati Oration)

Dr. Bhaskar Pal (Dr. S. K. Das Oration)

Conference 9th & 10th Aug, 2025 at India Habitat Centre





स्वस्थ नारी सशक्त परिवार अभियान

"Public Awareness & स्वस्थ नारी सशक्त परिवार अभियान" on 17th September 2025 under the aegis of NARCHI Delhi Chapter organized by Institute of Obstetrics & Gynaecology, Sir Ganga Ram Hospital.

We were blessed by our chief guests Dr. Jayashree Sood, About 80 delegates participated in this event. This endeavor was highly appreciated and requests came for more such activities in future.

The speakers like Dr. Kanwal Gujral who spoke on "Overview of the Cancer & Program", Dr. Mala Srivastava's topic was on "Prevention of breast carcinoma" & Dr. Chandra Mansukhani's topic was on "Prevention of Carcinoma Endometrium", Dr. Mamta Dagar's topic was on "Prevention of Carcinoma Cervix", Dr. Renuka Brijwal's topic was on "Prevention of Ovarian Carcinoma Cancer"

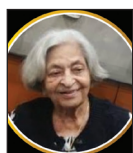


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