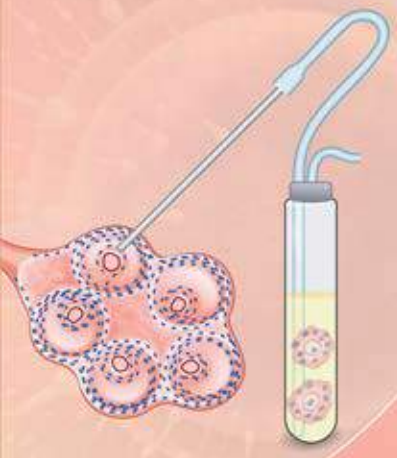

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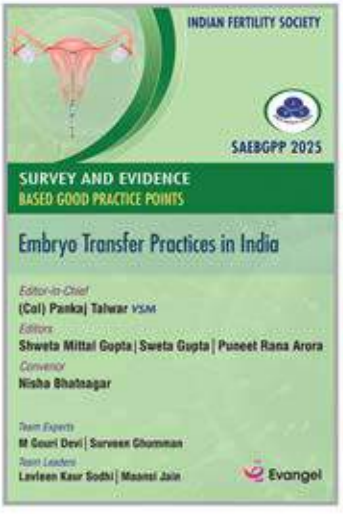
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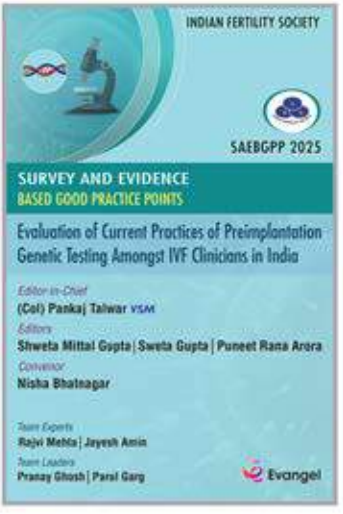
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Survey and Evidence Based Good Practice Points

Ovarian Stimulation

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SAEBGPP 2025

Survey and Evidence Based Good Practice Points

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Dedicated to

All gynecologists of India—those who continue to serve with compassion, courage, and commitment; those who balance science with empathy; those who stand by their patients through hope, uncertainty, and healing; and those who strive every day to raise the standards of women's health and reproductive care in our country.

Your tireless efforts inspire this entire initiative.

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Preface

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The SAEB (Survey and Evidence-Based) Good Practice Points initiative was conceived with the vision of bringing together clinicians, embryologists, researchers, and educators across India to create practical, implementable, and ethically sound guidelines that address real-world challenges in reproductive medicine. Each chapter in this compendium represents months of dedicated teamwork, data collection, expert deliberation, and collaborative refinement.

An important driving force behind this initiative has been the vision of the IFS President, who recognized the prevailing lacunae and knowledge gaps arising from the absence of India-specific recommendations. This endeavor reflects the commitment to develop guidance that is rooted in our own population data, clinical realities, and diversity of practice settings.

The strength of this work lies in its collective wisdom. By combining survey-driven insights with a rigorous evidence-based approach, we have attempted to bridge the gap between everyday clinical practice and evolving scientific knowledge. These GPP documents are not meant to replace existing guidelines; rather, they aim to complement them by offering context-specific recommendations tailored to the Indian ART landscape.

It is our hope that this consolidated effort will support clinicians in making informed decisions, encourage uniformity of care, and ultimately contribute to improved patient outcomes. We extend our gratitude to everyone who contributed to this initiative and made this work possible.

Acknowledgments

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We thank the reviewers, statisticians, and mentors who provided constructive feedback at every stage, ensuring that each chapter meets the highest academic and practical standards. Special appreciation is extended to the editorial and organizational teams whose behind-the-scenes efforts—coordination, communication, formatting, plagiarism checks, and preparation of final deliverables—were indispensable.

To every participant who contributed time, expertise, and passion: this work stands as a testament to your dedication to improving ART practice in India.

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Contents

Ovarian Stimulation

INTRODUCTION

Ovarian stimulation is a central component of assisted reproductive technology, aiming to achieve controlled multifollicular development while safeguarding patient safety. We have witnessed a shift from long agonist protocol to the more convenient antagonist protocol as the main stay of the majority of ovarian stimulation in the last decade. Current focus is to shift towards patient tailored treatment protocols. Newer protocols such as Duostim and Luteal phase stimulation have shown promising results, while the need for hormonal monitoring during an IVF cycle is being questioned.

We have integrated evidence from across the globe with what is currently being practiced by our Indian doctors to create these recommendations. The Indian survey was conducted in 2025 and 30% of the participating doctors have had more than 10 years of experience in infertility treatment and another 26% have had more than 5 years of experience. Almost two third of these doctors are working in private setup and a fourth in corporate organization. These guidelines intend to summarize current knowledge while identifying gaps that future research must address.

QUSTION 1 AND 2 OF THE SURVEY HAVE BEEN MENTIONED IN THE INTRODUCTION .

PICO 1: HORMONAL ASSESSMENT DURING OVARIAN STIMULATION

Does the addition of hormonal assessment during the stimulation cycle improve efficacy and safety in comparison to ultrasound only?

Recommendations

- Baseline evaluation of estradiol (E2) in women undergoing controlled ovarian stimulation (COS) for IVF/ICSI is not recommended due to lack of supporting evidence.
- Elevated baseline progesterone (P4) levels do not seem to impact IVF/ICSI cycle outcomes. Assessment of progesterone level on day 2 of the cycle at the start of ovarian stimulation is probably not recommended.
- The addition of E2 measurement to transvaginal sonography (TVS) monitoring is not recommended.
- The addition of a hormonal panel consisting of a combination of estradiol, progesterone, and LH measurements to ultrasound monitoring is not recommended.

SUMMARY OF EVIDENCE

Baseline Assessment

Estradiol

According to the European Society of Human Reproduction and Embryology (ESHRE) 2019 guidelines (updated 2025) for controlled ovarian stimulation, basal estradiol alone is not a predictor of ovarian response.[1] No recommendation can be given on the prognostic role of baseline estradiol (E2) in women undergoing COS for IVF/ICSI due to lack of supporting evidence.

A meta-analysis by demonstrated that basal estradiol has low accuracy in predicting poor ovarian response.[2] Subsequent studies have confirmed its limited predictive value.[3-5] The *American Society for Reproductive Medicine (ASRM)* further notes that the test has value only as an adjunct in the interpretation of normal basal serum follicle-stimulating hormone (FSH) levels.[6]

Progesterone

Progesterone (P4) is mainly synthesized by the corpus luteum during the luteal phase of the menstrual cycle, with levels reaching a nadir at the beginning of the next cycle unless rescued by human chorionic gonadotropin (hCG). Elevated P4 during day 3 is uncommon and may result from incomplete luteolysis, endogenous adrenal P4 production, or ovarian aging.

A comparative study evaluating outcomes between women with normal (P4 <1.5 ng/mL) and elevated baseline progesterone (P4 ≥ 1.5 ng/mL) levels undergoing IVF with a GnRH antagonist protocol coupled with PGT-A (NGS) found no difference

in oocyte yield, maturity rates, embryo quality, or euploidy rates. The prevalence of elevated baseline P4 (EBP) was 1.2%.[7]

A 2014 meta-analysis showed that elevated P4 levels before stimulation were associated with a 15% lower pregnancy rate in fresh day-3 transfer cycles. However, given the low incidence (6.7%) and lack of effective intervention, routine P4 screening was not recommended.[8]

A more recent 2024 meta-analysis on fresh COS cycles found that elevated baseline P4 did not impact live birth or clinical pregnancy rates (CPR).[9]

Hormonal Measurement During COS

Monitoring of the COS cycle is necessary to prevent ovarian hyperstimulation syndrome (OHSS), achieve an optimal ovarian response, and determine the appropriate time to trigger final follicular maturation. The goal is to maximize success in assisted reproduction treatment (ART) while avoiding complication such as OHSS.

Traditionally, COS during IVF/ICSI treatment has included combined monitoring using transvaginal sonography (TVS) plus serum E2 levels. However, the need for combined monitoring remains controversial. Opponents argue that it is time-consuming, expensive, and inconvenient for women, suggesting that simplified monitoring using transvaginal sonography (TVS) alone should be considered.[1]

A Cochrane review included six studies—four using GnRH agonist protocols exclusively and two including both GnRH agonist and antagonist regimens. Therefore, it remains unclear whether these findings apply to GnRH antagonist-only cycles.[10]

This meta-analysis found no advantage of combined TVS and E2 monitoring over TVS-only monitoring in terms of clinical pregnancy rates or OHSS incidence. The number of oocytes retrieved was comparable between both protocols. Both approaches were considered safe and reliable.

A meta-analysis including 797 women across six studies compared monitoring COS using TVS alone versus TVS combined with hormonal assessment. Among these, 359 women were monitored using TVS only, and 366 using combined hormonal monitoring.[11]

The study concluded that TVS-only monitoring is unlikely to substantially alter the chances of achieving clinical pregnancy (low-quality evidence). The number of oocytes retrieved was similar between both groups (moderate-quality evidence). The effect on OHSS incidence was uncertain, and no study reported live birth outcomes.

A single-center retrospective cohort assessed serum P4 and E2 levels on the day of trigger and found no adverse impact of elevated progesterone (>1.5 ng/mL) on pregnancy outcomes.[12] Hormonal profiles and rates of progesterone elevation were comparable between those who conceived and those who did not, suggesting that preovulatory sex steroid levels are not the primary determinant of ART outcomes across ovarian response categories.[12]

Despite the lack of strong evidence for benefit, a cross-sectional global survey revealed that the majority of ART specialists consider hormonal monitoring as essential, and that ~80% of ART specialists continue to use hormonal monitoring in addition to TVS, primarily for OHSS prevention, regardless of the added cost.[13]

Research Gap

There is currently no globally accepted guideline for COS monitoring, resulting in inconsistency in clinical reporting and research design. Considerable heterogeneity among studies, likely due to differences in stimulation protocols, may influence outcomes.

Further well-designed studies are required to evaluate and standardize the optimal monitoring strategy for COS in IVF/ICSI cycles.

Survey Result

Q3. How often do you perform baseline hormonal assessment in addition to ultrasound before starting the stimulation?

Choices	Percentage	Count
Always	49.87%	190
Individualized	46.46%	177
Never	3.67%	14
	Total	381
	Unanswered	4

Analysis of performing baseline hormonal assessment in addition to ultrasound before starting the stimulation.

Q 4. How often do you add testing for serum estradiol and/or serum LH levels in addition to ultrasound monitoring during COS?

Choices	Percentage	Count
In all cases	38.36%	145
In hyper-responders	25.66%	97
Never	20.11%	76
In poor responders	15.87%	60
	Total	378
	Unanswered	7

Analysis of testing for serum estradiol and/or serum LH levels in addition to ultrasound monitoring during COS

Integration with Evidence

Although current guidelines and evidence do not routinely recommend the use of hormonal assay along with ultrasound monitoring, majority of clinicians are advising it in all cases.

PICO 2: ROLE OF HORMONAL PRETREATMENT

Does hormonal pretreatment improve the efficacy of ovarian stimulation?

Recommendations

Oral Contraceptive Pill (COCP) Pretreatment

- Not recommended in GnRH antagonist cycles due to reduced live birth and ongoing pregnancy rates.
- May be used for cycle scheduling, but allow a 5–7-day washout period to prevent over suppression.

Progesterone Pretreatment

- Cannot be recommended to improve pregnancy outcomes in agonist or antagonist cycles.

- May be used for cycle scheduling as it has no negative impact on outcomes and may reduce ovarian cyst formation.

Estrogen (Luteal Estradiol) Pretreatment

- Recommended in low ovarian reserve patients to improve oocyte yield in GnRH antagonist cycles.
- Can be used for scheduling in antagonist cycles.
- Not recommended in GnRH agonist cycles due to lack of benefit.

GnRH Antagonist Pretreatment

- Not recommended routinely as it shows no significant improvement in clinical outcomes.
- May improve follicular synchronization in poor responders but does not translate into higher live birth rates (LBRs).

Summary of Evidence

COCP Pretreatment

In an earlier meta-analysis of six RCTs (1,343 patients) by *Griesinger et al.,* 2010:[14] COC pill usage showed lower pregnancy rates and increased gonadotropin usage. However, later study[15] with moderate-quality evidence confirmed lower LBR/OPR in antagonist cycles; no significant difference in OHSS, multiple pregnancy, or cyst formation. In PCOS patients using a freeze-all strategy, no significant difference in embryo quality or LBR was revealed.[16]

Progesterone Pretreatment

There was[15] no significant effect on LBR/OPR was observed after progesterone pretreatment. Some benefit observed were reduced chances of ovarian cyst formation in GnRH agonist cycles, with no adverse effect on multiple pregnancy or pregnancy loss.

Estrogen Pretreatment

Evidence on estrogen pretreatment remains mixed and insufficient to guide clinical practice. Early retrospective data[17] suggested improved embryo quality and higher oocyte yield in antagonist cycles, but larger, higher-quality Studies and a meta-analysis[18]—found no significant effect on ongoing pregnancy or live birth rates, nor on OHSS or pregnancy loss. More recent data from also showed no overall benefit, with the exception of improved oocyte yield in Poseidon Group 4 patients.[19]

GnRH Antagonist Pretreatment

Evidence for GnRH antagonist pretreatment remains inconsistent and does not show a meaningful improvement in clinical outcomes. Early work[20] in poor responders reported better oocyte and embryo yield using the CRASH protocol, but this did not translate into higher clinical pregnancy rates. Subsequent studies, including[21,22] noted improved follicular or embryonic synchronization and a small rise in retrieved oocytes, yet no significant gains in clinical or live birth rates. More robust data from[23] in normo-ovulatory women similarly showed no benefit in oocyte yield or pregnancy outcomes.

Research Gap

Across pretreatment strategies, the evidence remains inconsistent due to heterogeneity in study design, patient selection, and outcome measures. These limitations make it difficult to determine whether estrogen or GnRH antagonist pretreatment offers any true clinical advantage or benefits specific subgroups. The lack of uniform, high-quality data highlights a clear research gap, emphasizing the need for large, well-designed, and standardized randomized controlled trials to establish the clinical value and appropriate indications for these pretreatment approaches.

Survey Result

Q5. Which pretreatment therapy do you use the most?

Choices	Percentage	Count
OC pills pretreatment	48.29%	184
Estrogen pretreatment	28.87%	110
None	15.75%	60
GnRH antagonist pretreatment	7.09%	27
	Total	**381**
	Unanswered	4

Analysis of pretreatment therapy do you used

Q6. Why do you use pretreatment?

Choices	Percentage	Count
To have a synchronous follicle development	61.58%	234
I don't use pretreatment	13.16%	50
To reduce the chance of cyst formation	13.16%	50
To schedule IVF cycles	12.11%	46
	Total	**380**
	Unanswered	5

Analysis of the use of pretreatment.

Q7. In your clinical experience how does pretreatment improve the efficacy of ovarian stimulation?

Choices	Percentage	Count
Better oocyte yield and more utilizable embryos	47.87%	180
Better scheduling of IVF cycles	29.52%	111
Not assessed	12.77%	48
No benefit seen	9.84%	37
	Total	**376**
	Unanswered	9

Analysis of the ways of improving the efficacy of ovarian stimulation

Integration with Evidence

Current clinical practice shows a significant disconnect from available evidence on hormonal pretreatment in ovarian stimulation. Nearly half of clinicians continue to use OCP pretreatment despite data showing reduced live birth and ongoing pregnancy rates in GnRH antagonist cycles, while only a small proportion use GnRH antagonist pretreatment, which is supported primarily for poor responders.

Although most clinicians prescribe hormonal pretreatment for follicular synchronization, evidence indicates that meaningful synchronization benefits are largely confined to poor responders. Similarly, many aim to improve oocyte or embryo yield with pretreatment, yet estradiol pretreatment—one of the few approaches shown to support these outcomes in poor responders—is underused. This mismatch between evidence and routine practice underscores the need for better dissemination of current data and the establishment of standardized, evidence-aligned protocols to improve IVF outcomes.

PICO 3: OPTIMAL PROTOCOL FOR OVARIAN STIMULATION

What Is the Optimal Protocol for Ovarian Stimulation?

Recommendation

GnRH antagonist protocols should be the default protocol in:

- High-risk OHSS patients (e.g., PCOS, high AMH)
- Fertility preservation cycles

GnRH antagonist protocol should be considered in:

- In General, for all patient due to comparable efficacy butr better safety profile.
- GnRH agonist long protocol may be considered for:
- Select poor responders due to better oocyte yield.

With advances in embryo freezing, vitrification, and individualized stimulation strategies, the antagonist protocol has emerged as a flexible and safer approach without compromising cumulative pregnancy or live birth outcomes.

Summary of Evidence

The choice of ovarian stimulation protocol—GnRH agonist (long protocol) versus GnRH antagonist—is pivotal in optimizing outcomes in IVF. Evidence synthesis indicates that GnRH antagonist protocols offer comparable pregnancy and live birth outcomes with a significantly lower risk of OHSS and shorter cycle duration, making them safer and more patient-friendly. GnRH agonist protocols, continue to remain valuable in specific subgroups (low ovarian reserve) due to better follicular synchronization and slightly higher oocyte yield. As per the available data, primary factors influencing protocol choice are – Age, Ovarian reserve (AMH, AFC), PCOS status, previous IVF response, need for fresh embryo transfer and OHSS risk.

Across multiple reviews and clinical trials, pregnancy outcomes appear largely comparable between GnRH agonist and antagonist protocols. Large analyses such as the Cochrane review and meta-analyses by[25,26] found no significant differences in clinical pregnancy or live birth rates. Individual studies—including Placido et al., (2006)[27] and Engmann et al., (2008)[28]—further support equivalence, showing

similar pregnancy outcomes even when comparing flexible antagonist approaches or different trigger strategies. Although Orvieto et al. (2013)[29] reported better outcomes with agonist protocols, this finding contrasts with the broader evidence base. Overall, clinical pregnancy rates remain essentially equivalent between the two stimulation strategies.

Evidence comparing oocyte yield between GnRH agonist and antagonist protocols shows minimal meaningful difference. Meta-analytic data from Franco[30,31] indicate comparable numbers of retrieved oocytes across protocols. Studies in specific populations, such as PCOS patients[32] also report similar oocyte counts, with the antagonist protocol offering lower OHSS and cancellation rates. While Huirne et al., (2007)[33] noted that antagonist cycles may produce one to two fewer oocytes due to early follicular asynchrony, this small difference does not affect pregnancy outcomes. Overall, agonist protocols may retrieve marginally more oocytes, but oocyte quality and downstream clinical results remain equivalent.

Across studies comparing GnRH agonist and antagonist protocols, live birth rates are generally equivalent when modern embryo-transfer strategies are used. Meta-analytic evidence from[34] demonstrates overlapping live birth probabilities between the two approaches, with the antagonist protocol offering the added benefit of lower OHSS risk. Subgroup analyses show some variation:[35] reported higher cumulative live birth rates with agonist protocols in poor responders, while outcomes were comparable in normo-responders;[36] suggested that patient age and ovarian reserve may influence protocol suitability; and[37] found similar cumulative birth rates overall, with obese women benefiting more from antagonist cycles. Other studies, including[38,39] further support broadly similar live birth outcomes across protocols. Overall, despite variability in individual study findings, the aggregated evidence indicates no meaningful difference in live birth rates between GnRH agonist and antagonist protocols.

Evidence consistently shows that GnRH antagonist protocols carry a significantly lower risk of OHSS compared with GnRH agonist protocols. Large RCT data from[40] demonstrated markedly higher rates of moderate and severe OHSS in agonist cycles, often necessitating a "freeze-all" strategy despite similar pregnancy outcomes. Multiple meta-analyses—including those by,[41,42] and the Cochrane review by[34]—confirm that antagonists reduce OHSS incidence across all severity grades and substantially lower the likelihood of hospital admission. Overall, the antagonist protocol is clearly superior in minimizing OHSS risk while maintaining comparable reproductive outcomes.

Research Gap

Further large-scale RCTs are warranted to compare oocyte yield across protocols.

Survey Result

Q8. What percentage of your IVF patients undergo a GnRH antagonist protocol?

Choices	Percentage	Count
More than 75%	48.66%	181
25–50%	24.46%	91
51–75%	17.20%	64
Less than 25%	9.68%	36
	Total	372
	Unanswered	13

Analysis of IVF patients undergo a GnRH antagonist protocol

Q9. What are the primary factors influencing your choice of protocols?

Choices	Percentage	Count
Age/ ovarian reserve/ previous stimulation response	68.95%	262
Patient age and Ovarian reserve	15.79%	60
Risk of OHSS	8.95%	34
Previous stimulation response	6.32%	24
	Total	380
	Unanswered	5

Analysis of primary factors influencing your choice of protocols

Q10. Based on your clinical experience, how does the GnRH antagonist protocol compare to the GnRH agonist protocol in terms of?

A. Pregnancy Rate

Choices	Percentage	Count
Equivalent	74.29%	286
Superior	14.81%	57
I have not evaluated	7.27%	28
Inferior	3.64%	14
	Total	385

B. Number of Retrieved Oocytes

Choices	Percentage	Count
Equivalent	63.12%	243
Higher	17.92%	69
Lower	10.13%	39
I have not compared	8.83%	34
	Total	385

C. Live Birth Rate

Choices	Percentage	Count
Equivalent	75.32%	290
Not assessed	11.17%	43
Superior	10.91%	42
Inferior	2.60%	10
	Total	385

D. Incidence of Ovarian Hyperstimulation Syndrome (OHSS)

Choices	Percentage	Count
Lower	51.17%	197
Equivalent	38.18%	147
I have not compared	7.01%	27
Higher	3.64%	14
	Total	385

Integration with Evidence

Survey data indicate that approximately 48% of clinicians report using GnRH antagonist protocols in over 75% of their IVF patients. The primary determinants influencing protocol selection include age, ovarian reserve, and previous stimulation response, reflecting individualized clinical decision-making approaches.

Most clinicians observed that the GnRH antagonist protocol yields pregnancy rates equivalent to the GnRH agonist protocol, which aligns with current evidence demonstrating broadly comparable clinical pregnancy rates between the two.

While the majority of clinicians reported a similar number of oocytes retrieved with both protocols, existing literature suggests that the GnRH agonist protocol may yield a slightly higher oocyte count—a finding that highlights a minor divergence between clinical perception and evidence.

Importantly, 75% of clinicians acknowledged that live birth rates are equivalent between the two protocols when modern freeze-all or cumulative embryo transfer strategies are employed, consistent with current high-quality meta-analyses.

Furthermore, the majority of respondents reported a lower incidence of OHSS in antagonist cycles, corroborating strong evidence favouring GnRH antagonist protocols as the safer option with equivalent efficacy and improved patient safety profiles.

PICO 4: ALL ABOUT GONADOTROPINS

What is the Optimal Dose and Type of Gonadotropins?

Q11. Which ovarian reserve tests do you primarily rely on for determining individualized gonadotropin dosing?

Recommendation

AMH and AFC are the most validated and widely accepted biomarkers for predicting ovarian response and should be used as primary guides for individualized gonadotropin dosing. Age, BMI, and previous response can supplement but not replace AMH/AFC-based assessments.

Summary of Evidence

AMH and AFC consistently emerge as the strongest predictors of ovarian response and are more accurate than age, BMI, or previous cycle performance. Studies by[39,40] highlight that both markers reliably identify poor and excessive responders, allowing clinicians to individualize stimulation protocols. AMH offers objective measurement but lacks international assay standardization, whereas AFC is quick and noninvasive but operator-dependent. Meta-analytic evidence from Toftager et al. further confirms the superior predictive accuracy of AMH, and[41] corroborate that both AMH and AFC outperform traditional predictors in guiding controlled ovarian stimulation. Overall, these markers are valuable tools for optimizing treatment strategies.

Survey Results

Q12. Which ovarian reserve tests do you primarily rely on for determining individualized gonadotropin dosing?

Choices	Percentage	Count
Age/AFC/Age/BMI/ previous ovarian response	72.30%	274
Anti-Müllerian hormone (AMH) and antral follicle count (AFC)	14.78%	56
Age and BMI	7.12%	27
Previous ovarian response	5.80%	22
	Total	**379**
	Unanswered	6

Analysis on the type of ovarian test used

Research Gaps

Key gaps persist in applying AMH and AFC to guide ovarian stimulation. There are no standardized thresholds to reliably classify patients into response categories, and AMH interpretation remains limited by assay variability. Additionally, integrated prediction models that combine AMH, AFC, and clinical factors are still underused in routine practice. Standardization and wider adoption of multivariable tools are needed to improve individualized treatment planning.

Integration with Evidence

The majority of clinicians (72%) base dosing decisions on a combination of AMH, AFC, and previous response, which is consistent with current evidence and guideline recommendations for individualized gonadotropin dosing and monitoring tool.

The preference for combining recombinant FSH with hMG among most clinicians is coherent with the current literature supporting similar efficacy with added benefits in certain patient populations.

Q13. What is your preferred gonadotropin in conventional IVF?

Recommendation

r- FSH alone, hp-HMG alone or Recombinant FSH along with hp-HMG are probably equally recommended .The cost ,availability & patient preference should be considered for individualized choice.

Summary of Evidence

In a meta-analysis by Bordewijk et al (2019)[42] it was seen that that recombinant FSH or hp – HMG achieve comparable live birth rate. Clinical pregnancy and live birth rates were slightly lower with rFSH compared to HP-hMG, but cumulative live birth rates were similar. Decision-making on gonadotropin choice should be based on convenience, availability, cost, and patient preference.

Witz et al, 2020[43] in a randomized controlled trial evaluated the efficacy and safety of highly purified hMG (150 IU) versus r-hFSH (150 IU) for ovarian stimulation with a GnRH antagonist protocol in a cohort of patients anticipated to be high responders(AMH ≥5 ng/mL. Cumulative live birth rates per cycle initiation were 50.6% in patients treated with hMG and 51.5% in those treated with r-hFSH (difference: -0.8%, 95% CI -8.7% to 7.1%). Live bith rate after fresh/ frozen embryo transfer were comparable with both agents.

Regarding the combination of rFSH & hp-HMG ,an RCT done in 2019 by Shu et al compared the clinical efficacy of very pure hMG (75 IU) combined with r-hFSH (75-

150 IU; n=305) with rFSH alone (150-225 IU; n=305) on ovarian stimulation for IVF in the long-term GnRHa regimen.[44] The number of MII oocytes retrieved, clinical pregnancy rate per begun cycle, or moderate/severe OHSS were not substantially affected by ovarian stimulation with or without hMG supplementation.

In an RCT by Qiu J et al. 2023, they assessed group 4 Bologna poor responders using the long GnRH agonist or GnRH antagonist protocol, they compared whether adding hMG (75 IU; n = 78) to rFSH (225-300 IU) during the early follicular phase of ovarian stimulation improves clinical outcomes compared to no supplementation.[45] For both the groups ongoing pregnancy rate per completed cycle and the clinical pregnancy rate per completed cycle), there was no discernible difference between hMG supplementation and no supplementation.

Research Gaps

Inconsistent outcomes in subgroup analyses, particularly in poor responders has been reported. Additionally, there is a need for more data on cost-effectiveness in low- and middle-income countries (LMICs).

Survey Results

Choices	Percentage	Count
Combination of recombinant FSH and hHMG	65.78%	246
Recombinant FSH +/- Recombinant LH	12.57%	47
Urinary FSH and hMG	12.57%	47
Only hMG	9.09%	34
	Total	**374**
	Unanswered	11

Analysis on use of type of gonadotrophin in conventional IVF treatment

Integration with Evidence

The preference for combining recombinant FSH with hMG among most clinicians is coherent with the current literature supporting similar efficacy with added benefits in certain patient populations.

Q14. What is your preferred starting dose of gonadotropin for a hyper-responder patient?

Recommendation

The optimal starting dose for hyper-responders is *100–200 IU* to minimize the risk of OHSS while maintaining adequate oocyte yield.

Summary of Evidence

For hyper-responders, initiating stimulation with 100–150 IU reduces OHSS risk without compromising efficacy and doses above 225 IU offer no additional benefit. This approach is supported by[47,48] who demonstrated that low starting doses maintain both safety and efficacy.[49] further confirmed that increasing gonadotropin doses beyond 200 IU does not improve live birth rates in this population.[50]

Research Gaps

Key gaps remain in optimizing low-dose stimulation for hyper-responders. There is limited long-term data on cumulative live birth rates with low-dose protocols, and evidence on individualized dosing specifically for PCOS-related hyper-responders is still sparse. More targeted, long-term studies are needed to guide refined dosing strategies in these populations.

Survey Results

Choices	Percentage	Count
100–200 IU	55.59%	209
225 IU	28.19%	106
75 IU	13.03%	49
300 IU	3.19%	12
	Total	376
	Unanswered	9

Analysis of starting dose of gonadotropin for a hyperresponder patient

Integration with Evidence

Clinical practice trends align well with the evidence supporting conservative dosing to prevent OHSS without reducing success rates.

Q15. What is your preferred starting dose of gonadotropin for a poor-responder patient?

Recommendation

Starting doses of *300–450 IU* are appropriate for poor responders. Doses above 450 IU rarely improve outcomes and increase cost without benefit. Mild individualized dose escalation based on AMH and AFC is preferred.

Summary of Evidence

Evidence in poor responders shows that increasing gonadotropin doses above a certain threshold offers no meaningful benefit.[49] in a Cochrane review, found no advantage with doses exceeding 450 IU/day, and[50] described a plateau in oocyte yield at higher doses. Further highlighted the importance of individualized, evidence-based dosing to avoid unnecessary cost and adverse effects, reinforcing a more tailored approach for this population.[51]

Research Gaps

Key gaps in managing poor responders include the absence of standardized definitions for "poor response," a lack of direct comparisons between commonly used high-dose regimens (300, 450, and 600 IU), and limited cost-effectiveness data specific to Indian clinical settings.

Survey Results

Choices	Percentage	Count
300 IU	61.07%	229
225 IU	20.53%	77
450 IU	16.80%	63
600 IU	1.60%	6
	Total	375
	Unanswered	10

Analysis of preferred starting dose of gonadotropin for a poor-responder patient

Integration with Evidence

The observed clinical practice of moderate high-dose gonadotropin stimulation (300–450 IU) corresponds well with evidence-based recommendations and reflects prudent, individualized patient management.

PICO 5: TRIGGER FOR FINAL OOCYTE MATURATION

Q16. Which trigger do you prefer in high responders (e.g., patients with high risk of OHSS)?

Recommendation

GnRH agonist trigger is strongly recommended for final oocyte maturation in women at high risk of OHSS. hCG trigger alone should *never* be used in patients with a previous history or risk of OHSS. Dual or agonist-only triggers are preferred in such cases.

Summary of Evidence

Ovarian hyperstimulation syndrome (OHSS) is an iatrogenic complication of controlled ovarian stimulation, primarily induced by hCG trigger. hCG increases VEGF responsiveness in granulosa cells, leading to excessive vascular permeability—resulting in third-space fluid shifts, thrombosis, and organ hypoperfusion.

Key predictors of OHSS include age, AMH, BMI, AFC, serum estrogen on trigger day, follicle number, and prior OHSS history.

The *ESHRE guidelines* (1) strongly recommend GnRH agonist trigger for women at risk of OHSS, when GnRH agonist trigger with a freeze-all strategy is not used, the choice between 5000 IU hCG and GnRH agonist remains debatable. GnRH agonist trigger should be followed by luteal phase support with LH activity. Historically, hCG was used for final oocyte maturation, but agonist triggers were introduced to prevent OHSS. Although GnRH agonists induce physiological LH and FSH surges, they may cause early luteolysis, leading to poor outcomes in fresh transfers. Dual trigger (GnRH agonist + low-dose hCG) balances efficacy and safety. A retrospective study comparing dual trigger vs. hCG alone in high responders found significantly lower moderate-to-severe OHSS rates in the dual trigger group, with no difference in live birth rate.[52] Similarly, retrospectively analyzed 2778 ART cycles and concluded that dual-trigger regimens effectively mitigate OHSS risk in high ovarian responders.[53]

Research Gap

Recognizing the pivotal role of the endocrine environment in influencing pregnancy outcomes and the occurrence of OHSS, further exploration of different triggering regimens is needed to optimize IVF outcomes and reduce OHSS risk.

Survey Result

Choices	Percentage	Count
GnRH agonist trigger only	63.73%	239
Dual trigger (hCG + GnRH agonist combined)	23.73%	89
Standard hCG trigger only	8.27%	31
Low dose hCG trigger	4.27%	16
	Total	375
	Unanswered	10

Analysis of the prefer in high responders

Integration with Evidence

GnRH agonist trigger remains the preferred strategy among most clinicians, aligning with ESHRE recommendations.

23% of clinicians report using a dual trigger for high responders, consistent with recent analyses (post-2019) supporting improved safety and oocyte maturation outcomes.

Q17. For patients with a history of suboptimal oocyte maturation, which trigger do you find most effective?

Recommendation

GnRH agonist induces a physiological surge of both LH and FSH, enhancing oocyte maturation compared to hCG, which mimics only LH.

Therefore, *dual trigger* should be used in patients with a history of suboptimal oocyte maturation (low MII oocyte yield).

Summary of Evidence

In an RCT normoresponders receiving dual trigger had significantly higher numbers of retrieved oocytes, MII oocytes, and zygotes than those receiving hCG alone.[54] Age and AMH was comparable between both the groups. The total amount of gonadotropins, the length of the stimulation and the number of follicles >10 mm

and >15 mm in diameter on day of hCG administration were also similar in the two groups. Dual trigger may potentially improve the outcome in IVF cycle.

A *systematic review by Lun Hu et al.*, involving 1048 studies showed dual trigger was associated with higher oocyte yield, mature oocyte rate, usable embryos, live birth rate, and implantation rate (2021).[55]

Similarly, found dual trigger improved fertilization rate, clinical pregnancy rate, and reduced cancellations in women with diminished ovarian reserve.[56] The optimal interval between GnRH agonist and hCG triggers varies as reported hCG is associated with a shorter interval to maximal MII retrieval.[57]

Research Gap

Triggering with GnRH-a has become a significant part of contemporary ART practice, especially in high responders, oocytes donors and oncology patients. However, more RCTs are required in order to justify the use of GnRH-agonists in poor responders in ART cycles.

Survey Result

Choices	Percentage	Count
Dual trigger	67.02%	252
Double trigger	13.56%	51
HCG trigger	11.97%	45
GnRH agonist trigger	7.45%	28
	Total	376
	Unanswered	9

Analysis of use of trigger in patients with suboptimal oocyte maturation

Integration with Evidence

Our survey findings align with global data favoring *dual trigger* in suboptimal oocyte maturation, suggesting a paradigm shift toward combined trigger strategies for better outcomes in GnRH antagonist cycles.

Q18. What are the key factors influencing your choice of trigger for final oocyte maturation?

Recommendation

Trigger selection should be individualized based on:

- Follicle count on trigger day
- Serum estradiol level
- Patient response (high/normo/poor)
- Previous oocyte maturation performance

Summary of Evidence

Types of Triggers

Type	Mechanism/dose	Advantages	Disadvantages
hCG (urinary or recombinant)	Mimics LH surge [u-hCG 5000 IU/r-hCG 250 µg (6500 IU) 36 hours prior to OPU]	Widely available, cost-effective	High OHSS risk due to prolonged half-life
r-LH	Shorter half-life, more physiological (27,000 IU, 32-34 hours prior to OPU)	Lower OHSS risk	Expensive, limited availability, NOT USED Clinically as trigger
GnRH agonist	Induces endogenous LH + FSH surge (Flare effect)(Triptorelin 0.2 mg s/c, Leuprolide 1 mg s/c, Buserelin 0.5 mg nasal 36 hours prior to OPU)	Minimizes OHSS, physiologic response	Requires antagonist protocol; luteal support essential
Dual trigger	GnRH agonist + low-dose hCG (1500 IU) 36 hours prior to OPU	Improved oocyte maturity, blastulation, pregnancy rates	Slight OHSS risk

GnRH agonist triggering offers several important clinical advantages.[58] demonstrated that an agonist trigger induces a shorter, more physiological LH and FSH surge, effectively reducing the risk of OHSS.[58] Building on this,[59] reported that when an agonist trigger is paired with a freeze-all strategy, OHSS risk can be completely eliminated due to rapid corpus luteum demise.

Retrospective analyses by[60,61] further support the value of a dual-trigger regimen, showing improved oocyte yield and oocyte acquisition rates, along with fewer transfer cancellations, particularly in high and normo-responders. Dual trigger has also shown remarkable benefit in patients with a history of poor oocyte maturation:[62] found dramatic improvements in the number of retrieved oocytes, MII oocytes, and

top-quality embryos among individuals with a low Follicular Output Index. A similar pattern was observed in an RCT by[63] where poor responders receiving 10,000 IU hCG plus 0.2 mg GnRH agonist obtained more MII oocytes, fertilized oocytes, and embryos than those receiving standard hCG alone; although the higher chemical and clinical pregnancy rates in the dual-trigger group were not statistically significant, the trend favoured combined triggering.

In terms of safety, ASRM highlights that rapidly rising serum estradiol levels are strong predictors of OHSS,[64] and studies[65] indicate that E2 levels exceeding 4,000–6,000 pg/mL, more than 35 intermediate follicles on trigger day, or retrieval of over 30 oocytes markedly elevate the risk of severe OHSS. Conversely, cycles with E2 <3,500 pg/mL or retrieval of fewer than 20 oocytes carry almost negligible risk. For this reason, GnRH agonist trigger is recommended for patients with rapidly rising estradiol levels, serum E2 >2,500 pg/mL, or the presence of numerous intermediate-sized follicles.

Survey Results

Choices	Percentage	Count
Number of follicles, Serum estradiol before trigger, Oocyte maturation rate in previous cycles	65.78%	246
Number of follicles	15.78%	59
Serum estradiol before trigger	9.89%	37
Oocyte maturation rate in previous cycles	8.56%	32
	Total	**374**
	Unanswered	11

Analysis of the key factors influencing choice of trigger for final oocyte maturation

Integration with Evidence

The survey indicates that clinicians are largely adopting *individualized trigger protocols*, consistent with global recommendations emphasizing OHSS prevention and optimization of oocyte maturity.

PICO 6: MILD VS. CONVENTIONAL STIMULATION PROTOCOLS

What is the role of Minimal Stimulation protocol in current practice?

Recommendation

In women with normal ovarian reserve, a *conventional stimulation protocol* remains the preferred approach. However, an individualized strategy may be considered in specific situations such as financial limitations, previous adverse responses, or patient preference.

Mild stimulation can be considered for reducing treatment-related stress, improving tolerance, and minimizing cost.

Summary of Evidence

Mild ovarian stimulation for IVF is defined as a protocol in which the ovaries are stimulated with gonadotrophins and/or other pharmacological agents with the intention of limiting the number of oocytes obtained. Practically, it involves daily gonadotrophin doses of ≤150 IU, with or without clomiphene citrate or letrozole, typically within a GnRH antagonist cycle.[66] The choice of mild stimulation is often driven by patient preference, the desire to minimize injections, or specific clinical situations, including a high risk of OHSS, clotting disorders, hormone-sensitive malignancies, or a history of poor response. Mild stimulation has also been linked to fewer psychosomatic side effects, better patient tolerance, and lower dropout rates compared with conventional protocols.[67]

Despite these advantages, routine use of mild stimulation in women with normal ovarian reserve is not supported by current evidence. Higher cancellation rates and reduced oocyte yield remain important limitations.[68] Because the number of oocytes retrieved is the strongest predictor of live birth, and no proven method exists to enhance oocyte quality, maximizing oocyte yield continues to be the most practical strategy for improving outcomes and compensating for age-related declines in embryo competence.[67,69] have highlighted that mild stimulation may enhance global access to IVF, especially in low-resource settings where intensive monitoring is not feasible. However,[69] emphasize that mild protocols should not replace conventional stimulation, as the lower oocyte yield is not offset by improved oocyte quality. Similarly,[68] noted that although mild stimulation reduces stress and cost, its uptake has been limited due to concerns about clinical efficacy.

Evidence synthesized by[68,70] suggests that mild stimulation IVF (≤150 IU/day with or without clomiphene citrate or letrozole) is a viable option for poor responders, offering comparable pregnancy outcomes and acceptable cancellation rates at lower cost (Level 1a evidence). In normal and high responders, mild

stimulation with ≤150 IU/day letrozole combined with an agonist trigger has been shown to maintain similar pregnancy outcomes with significantly lower OHSS risk (Level 1b+, moderate QoE). Although fewer oocytes and embryos are generated with mild stimulation, the proportion of high-grade embryos remains similar to conventional stimulation. For hyper-responders at very high risk of OHSS, in-vitro maturation (IVM) may serve as an alternative in selected cases (two RCTs, moderate QoE).

Overall, mild stimulation is more patient-friendly and cost-effective, but uncertainties regarding pregnancy outcomes and cycle cancellation rates have limited its broader acceptance.[67,71] Further reported that cumulative live birth rates remain comparable between mild and conventional stimulation, despite a higher number of oocytes and embryos in the latter, suggesting that mild stimulation may still be appropriate for select low-prognosis patients

Research Gap

Further large-scale RCTs are needed to strengthen the evidence base for mild ovarian stimulation. Specifically, future research should clarify the optimal gonadotropin dosing strategy, compare outcomes across poor, normal, and hyper-responder groups, and evaluate long-term cumulative live birth rates in diverse patient populations.

Survey Findings

Q19. What percentage of women with normal ovarian reserve undergo mild stimulation in your practice?

Choices	Percentage	Count
Less than 25%	41.49%	156
25–50%	28.72%	108
None	26.06%	98
51–75%	3.72%	14
	Total	376
	Unanswered	9

Analysis of the women with normal ovarian reserve undergoing mild stimulation

Integration with Evidence

For women with normal ovarian reserve, mild stimulation is not routinely recommended, aligning with the observation that *31% of clinicians avoid it entirely,* while *41% use it in <25%* of cases.

Q20. What factors influence your decision to use mild stimulation protocols?

Survey Result

Choices	Percentage	Count
Cost primarily	27.39%	103
Previous poor response with conventional dose	25.27%	95
I don't use mild stimulation	24.73%	93
ovarian reserve	22.61%	85
	Total	376
	Unanswered	9

Analysis of the decision to use mild stimulation protocols

Integration with Evidence

Approximately 27% of clinicians cite treatment cost as a determining factor for selecting mild stimulation. This corresponds with global data emphasizing individualized, cost-sensitive approaches.

Q21. What do you use in cases of mild stimulation?

Survey Result

Choices	Percentage	Count
Both oral ovulogens and low dose gonadotropins	51.87%	194
I don't use mild stimulation	25.40%	95
Oral ovulogens only	11.76%	44
Low dose gonadotropins only	10.96%	41
	Total	374
	Unanswered	11

Analysis of the use in cases of mild stimulation

Integration with Evidence

While *10% of clinicians* reported using *low-dose gonadotropins alone*, the majority (*51%*) combine them with *oral ovulogens*.

This reflects evidence from multiple RCTs showing *MS-IVF (≤150 IU/day ± CC/letrozole)* achieves comparable pregnancy outcomes and cycle cancellation rate with lower medication burden and cost.

Q22. How do you rate outcomes of mild stimulation in your practice?

Survey Results

Choices	Percentage	Count
Lower medication costs	35.39%	132
I have not compared	34.58%	129
Better pregnancy rates	15.55%	58
Higher cancellation rates	14.48%	54
	Total	373
	Unanswered	12

Analysis of the outcomes of mild stimulation in practice

Integration with Evidence

Clinicians expressed cautious optimism but acknowledged the need for stronger data. Existing studies suggest mild stimulation is a *patient-friendly and economical alternative*, but larger trials are required to confirm its *effectiveness and reproducibility* in normoresponders.

PICO 7: DUAL STIMULATION (LUTEAL AND FOLLICULAR PHASES)

Recommendation

DuoStim is recommended for patients with *POR* to enhance total oocyte and embryo yield, thereby improving *cumulative pregnancy and live birth outcomes.*

Individualized assessment remains essential, particularly in women with POR, diminished ovarian reserve, or time-sensitive fertility needs.

DuoStim is useful for patients who might benefit from increasing the number of oocytes retrieved to maximize the cumulative live birth rate (CLBR) per intention-to-treat (ITT).

Summary of Evidence

Definition

Dual stimulation (DuoStim) involves performing two controlled ovarian stimulation cycles—one during the follicular phase (FPS) and another during the luteal phase (LPS)—within the same menstrual cycle. This strategy is increasingly adopted for poor ovarian responders (PORs), as it helps maximize the total number of oocytes retrieved, shortens the time required for embryo accumulation, and is especially valuable in fertility preservation and urgent ART scenarios. Evidence shows that luteal-phase stimulation is both safe and effective, with no adverse impact on embryo quality. Reported that using a GnRH agonist or recombinant hCG trigger, instead of urinary hCG, may yield a higher number of good-quality embryos in both FPS and LPS. Interestingly, the LPS phase often produces more oocytes and embryos than FPS in DuoStim cycles.[72]

Clinically, DuoStim is particularly advantageous for poor responders who need to maximize oocyte yield within a single cycle and for oncofertility patients requiring rapid oocyte cryopreservation.[73] The approach has demonstrated consistently positive outcomes, including higher total oocyte and embryo counts, reduced time to embryo accumulation, and improved cumulative live birth rates. It has also proven safe, reproducible, and beneficial for older women and those with diminished ovarian reserve when used with individualized stimulation protocols.

Research Gap

Further large, randomized controlled trials are needed to strengthen the evidence base for DuoStim. Such studies should focus on defining standardized stimulation and trigger protocols, evaluating long-term outcomes including live birth rates and obstetric safety, and determining the cost-effectiveness and overall safety of DuoStim across diverse patient populations.

Study	*Design*	*Finding*	*Implication*	*Outcome*
Ulbadi et al., 2024[74]	Review article in F&S	Pros—Decrease cost, drop out rate, time to pregnancy. Cons—Not enough evidence to use it	Consider in. women where more oocytes have to be retrieved in shorter span like cancer patients awaiting chemotherapy	
Vaiarelli et al., (Jan 2020)[75]	▪ Prospective observational ▪ Case series (conventional COS vs DuoStim)	Does not support that DuoStim is superior to two conventional COS protocols in terms of CLBR per ITT.	▪ Effective for POR patients ▪ Luteal phase after conventional stimulation in the same ovarian cycle might improve the management of poor responder patients	▪ DuoStim has Higher chance to obtain a euploid blastocyst and possibly higher clinical pregnancy rate ▪ Lessens the patient drop-out rate
Ubaldi et al., (2016)[76]	Observational	A double-stimulation approach within a single menstrual cycle (DuoStim) in a cohort of patients with POR. GnRH agonist was used for both FP and LP ovulation triggering	Stimulation with an identical protocol in the FP and LP of the same menstrual cycle resulted in a similar number of blastocysts in patients with reduced ovarian response	The LP stimulation statistically significantly contributed to the final transferable blastocyst yield, thus increasing the number of patients undergoing transfer per menstrual cycle
Luo et al. Oct, 2020[72]	Retrospective study		▪ Significantly higher number of oocytes retrieved, normal fertilized oocytes, cleaved embryos, cryopreserved embryos, and good quality embryos at the LPS stage than at the FPS stage ▪ Regardless of the stage, rhCG and GnRH-a yielded	The use of GnRH-a or rhCG as the trigger drug may be better than uhCG in both the FPS and LPS stages for POR undergoing the DuoStim protocol.

Contd...

Contd...

Study	Design	Finding	Implication	Outcome
			significantly more cryopreserved embryos and good quality embryos than uhCG	
Massin N et al., (2023)[77]	Multicenter, open-labelled RCT (DuoStim) vs two consecutive antagonist cycles in poor responders	The mean (SD) cumulative number of oocytes retrieved, mature oocytes and total embryos from two ovarian stimulations was not statistically different between the control and duostim groups	▪ Failed to demonstrate a superiority of DuoStim regarding the cumulative number of oocytes obtained, and mature oocytes ▪ The implantation rate was similar.	▪ Embryos obtained with DuoStim seems unimpaired ▪ No potentializing effect on the number of oocytes retrieved in the luteal phase after follicular phase stimulation
Yang et al. 2023[78]	Retrospective analysis comparing double ovulation stimulation (DouStim) with a conventional antagonist protocol in patients with diminished ovarian reserve and asynchronous follicular development	DouStim protocol resulted in more mature oocytes and high-quality embryos.	The DouStim group also showed better outcomes in embryo yield, blastocyst formation, implantation, and hCG-positive rates compared to the antagonist group	

Q23. Do you currently use dual stimulation (follicular and luteal phases) for patients with poor ovarian reserve?

Survey Findings

Choices	Percentage	Count
No	50.80%	190
Yes	49.20%	184
	Total	374
	Unanswered	11

Analysis of the use of dual stimulation (follicular and luteal phases) for patients with poor ovarian reserve

Integration with Evidence

Although the majority of clinicians in our survey are not routinely using DuoStim for poor responders, *49%* have adopted it in selected cases. This aligns with emerging evidence indicating that *DuoStim* is a promising strategy for *poor responders*, enabling *maximal oocyte retrieval within a single menstrual cycle*.

Q24. How do the outcomes of luteal-phase stimulation compare to follicular-phase stimulation based on your experience?

Recommendation

The initiation of ovarian stimulation during the luteal phase may be considered in selected populations, especially in women with POR or in the context of fertility preservation in oncology cases where time is a constraint.

Summary of Evidence

Protocol Description

Luteal-phase stimulation begins after ovulation, typically during the mid- to late luteal phase of the menstrual cycle. Similar to conventional IVF protocols, ovarian stimulation with FSH or hMG is continued for 8–15 days. GnRH antagonists are introduced when the lead follicle reaches approximately 14 mm in diameter or based on rising serum estradiol levels to prevent premature luteinization.[79]

During DuoStim cycles, abstinence or mechanical contraception is generally required in the follicular phase. After ovulation or follicular-phase oocyte retrieval, luteal-phase stimulation (LPS) can begin once at least one follicle reaches 6–11 mm, typically using 225 IU of hMG along with 2.5–5 mg of letrozole daily for five days.[80] A freeze-all strategy is standard practice, with cryopreservation of all viable embryos. Evidence comparing follicular-phase ovarian stimulation (FPOS) and LPS continues to expand. In a 2024 RCT involving 78 poor ovarian responders, reported that the LPS group produced significantly more MII oocytes ($p = 0.007$), although no differences were seen in GV or MI oocytes, top-quality day-3 embryos, or day-3 embryo development rates.[81] similarly showed that LPS performed comparably to FPS and may even enhance ovarian responsiveness in younger poor responders.[82]

More recent data reinforce these findings. A September 2025 retrospective cohort study in Fertility & Sterility showed that, once confounders such as fresh transfers and suboptimal endometrial receptivity were excluded, LPS yielded clinical and embryological outcomes comparable to FPS.[83] Clinical pregnancy rates were nearly identical between follicular (68.44%) and luteal (67.67%) stimulations (OR 0.975; 95% CI 0.751–1.266). While LPS required a higher total FSH dose (4,350.92 IU vs. 3,989.11 IU), stimulation duration was similar. FPS produced slightly more oocytes overall (12.61 vs. 11.85), yet paired analyses showed LPS generating more oocytes per patient (8.54 vs. 7.31). Among women under 35, blastocyst biopsy rates were higher in LPS cycles (61.01% vs. 55.37%). Oocyte maturation, fertilization, euploidy, and cumulative live birth rates were comparable across age groups and transfer attempts. Supporting this, a retrospective matched case-control study published in EJOG[84] found that although differences did not reach statistical significance, LPS showed favorable trends toward higher cumulative live-birth and clinical pregnancy rates. These data suggest that LPS may be a practical, cost-effective option—particularly for older women, those with diminished ovarian reserve, or patients with previous IVF failures.

Research Gap

Further studies are needed to standardize the timing, dosing, and trigger criteria for luteal-phase stimulation, as well as to evaluate long-term neonatal outcomes and assess the time and cost-effectiveness of this approach. Research should also focus on defining patient-specific protocols for poor responders and women of advanced age. Given the notable interpatient variability in the optimal timing of LPS initiation, high-quality randomized controlled trials are essential to harmonize protocols and improve consistency in clinical outcomes

Survey Results

Choices	Percentage	Count
No significant difference in outcomes	46.83%	170
Higher oocyte yield	29.20%	106
Improved embryo development	14.33%	52
Higher clinical pregnancy rate	9.64%	35
	Total	363
	Unanswered	22

Analysis of the outcomes of luteal-phase

Integration with Evidence

Majority clinicians reported that they do not find any significant difference in between the FPOS and LPOS, which is coherent with the current available evidence.

KEY GOOD PRACTICE POINTS

1. Baseline evaluation of estradiol and progesterone in women undergoing COS for IVF/ICSI is not recommended.
   According to Indian survey data, 49.8% of Indian specialist seem to use hormonal levels of estrogen and progesterone as guide to start stimulation on day 2 as well as during the cycle to monitor the COS cycle, even though current evidence suggests limited benefit of using hormonal measurement as monitoring tool.

2. Oral Contraceptive Pill (COCP) Pretreatment is not recommended due to reduced live birth and ongoing pregnancy rates. Progesterone pretreatment is not recommended to improve pregnancyoutcome. Estrogen (Luteal Estradiol) Pretreatment is recommended in low ovarian reserve patients to improve oocyte yield in GnRH antagonist cycles. GnRH Antagonist Pretreatment is not recommended routinely as it shows no significant improvement in clinical outcomes.

According to Indian survey data, Indian clinicians seem to rfavor the use of COC pills as pretreatment to allow for better cohort of follicles, with 61% of them using some form of pretreatment and 48% preferring COC, while 28% using luteal estrogen.

3. GnRH Antagonist protocol is recommended in patients with PCOS/ high risk of OHSS, fertility preservation and in general, for all controlled stimulation cycles. GnRH agonist may be used in selected patients with poor ovarian reserve.
   Indian Survey Data shows that 49.6%most clinicians prefer antagonist protocol in more than 75% of the stimulation cycles. Personalized COS is practiced using age, ovarian reserve and previous stimulation response as the guide to stimulation protocol. Also, perception of the Indian clinicians stands aligned with the international evidence as 79% of the clinicians say tha GnRH antagonist and agonist protocol yields similar results in term of oocyte yield and pregnancy rate while Antagonist protocol being safe in terms of reduced OHSS risk.

4. AMH and AFC are recommended biomarkers for predicting ovarian response. They can be further supplemented with age, BMI and previous response to stimulation when determining individualized gonadotropin dosing.
   According to Indian survey data, around two third Indian doctors (72.3%) prefer to use not only AMH &AFC, but also age ,BMI and response to previous ovarian stimulation

5. Recominant FSH alone, hp-HMG alone or Recombinant FSH along with hp-HMG are probably equally recommended .The cost ,availability & patient preference should be considered for individualized choice
   HMG and FSH during IVF stimulation. This is cost effective strategy as fertility treatment cost is borne by Indian consumers themselves.

6. It is recommended to use a starting dose of 100-150 IU in hyper responders as it reduces the risk of OHSS without compromising efficacy. It is advised that a starting dose of 300-450 IU is appropriate for poor responders.

   According to Indian survey data, Clinicians in India prefer an evidence-based practice and prudent individualized stimulation plan. 55.6% of the clinicians prefer to start with a dose of 100-200 in hyper responders and 61% of the clinicians say that they prefer to start with a dose of 300 IU for poor ovarian reserve.

7. Patients undergoing Antagonist stimulation, trigger selection is based on follicle count on the day of trigger, serum estradiol levels (if done), and previous oocyte maturation performance. In patients with high risk of OHSS, agonist trigger is strongly advocated. In patients with history of suboptimal oocyte maturation, use of dual trigger is recommended.
   It is also part of practice of most of the clinicians in India. GnRH agonist trigger remains the preferred strategy among most clinicians, aligning with ESHRE recommendations. According to Indian survey data, Dual trigger is used by 23% of the clinicians supporting safety and oocyte maturation outcomes.67% of Indian clinicians prefer to opt for dual trigger when facing history of suboptimal response in previous cycle.

8. Conventional full dose stimulation protocol is the preferred stimulation protocol. Mild stimulation protocol may be considered in selected circumstances as an alternative.
   According to Indian survey data, 42% of the clinicians prefer conventional stimulation over mild stimulation in patients with normal ovarian reserve consistent with the global opinion. Among those using it cost is often the determining factor in 27% and poor previous response to conventional stimulation in 25% of the clinicians. . It is often combined with oral ovulogens by 52% of the clinicians when opting for mild stimulation.

9. *DuoStim* is recommended for patients with POR to enhance total oocyte and embryo yield, thereby improving cumulative pregnancy and live birth outcomes. Individualized assessment remains essential, particularly in women with POR, diminished ovarian reserve, or time-sensitive fertility needs.
   According to Indian survey data, 50% of the clinicians have started to adopt duostim in selected population(among patients with poor ovarian reserve). It is among the newer treatment protocols and have shown promising benefits while decreasing the psychological distress to patients. More studies and experience is needed to understand its impact.

10. Luteal phase stimulation may be used for ovarian stimulation in selected patients with poor ovarian reserve and in context to fertility preservation.
    According to Indian survey data, 46% of the clinicians have seen no difference in the stimulation outcome in terms of oocyte yield and pregnancy rate. 29% of the clinicians report better oocyte yield with luteal phase stimulation more robust data and experience is required for future recommendations.

11. Luteal phase stimulation may be used for ovarian stimulation in selected patients with poor ovarian reserve and in context to fertility preservation. *According to Indian survey data, 46% of the clinicians have seen no difference in the stimulation outcome in terms of oocyte yield and pregnancy rate. 29% of the clinicians report better oocyte yield with luteal phase stimulation more robust data and experience is required for future recommendations.*

SURVEY QUESTIONNAIRE OF OVARIAN STIMULATION

1. How many years of experience do you have in IVF treatment ?
   a. Less than 5 years
   b. 5–10 years
   c. More than 10 years
   d. Under training
2. Type of organization, in which you practice -
   a. Government
   b. Corporate
   c. Private
   d. Semigovernment/Trust hospital /PPP hospital
3. How often do you perform baseline hormonal assessment in addition to ultrasound before starting the stimulation?
   a. Always
   b. Individualised
   c. Never
4. How often do you add testing for Serum Oestradiol and/or Serum LH levels in addition to ultrasound monitoring during COS?
   a. In all cases
   b. Never
   c. In hyper responders
   d. In poor responders
5. Which pre-treatment therapy do you use the most ?
   a. Oestrogen pre-treatment
   b. OC pills pre-treatment
   c. GnRH antagonist pre-treatment
   d. None
6. Why do you use pre- treatment?
   a. To schedule IVF cycles
   b. To have a synchronous follicle development

c. To reduce the chance of cyst formation
d. I don't use pre-treatment

7. In your clinical experience how does pre-treatment improve the efficacy of ovarian stimulation?
   a. Better oocyte yield & More utilizable embryos
   b. Better scheduling of IVF cycles
   c. Not assessed
   d. No benefit seen
8. What percentage of your IVF patients undergo a GnRH antagonist protocol?
   a. Less than 25%
   b. 25–50%
   c. 51–75%
   d. More than 75%
9. What are the primary factors influencing your choice of protocol?
   a. Patient age and Ovarian reserve
   b. Risk of OHSS
   c. Previous stimulation response
   d. Both a & c
10. Based on your clinical experience, how does the GnRH antagonist protocol compare to the GnRH agonist protocol in terms of:
   A. Pregnancy rate
      a. Superior
      b. Equivalent
      c. Inferior
      d. I have not evaluated
   B. Number of retrieved oocytes
      a. Higher
      b. Equivalent
      c. Lower
      d. I have not compared
   C. Live birth rate
      a. Superior
      b. Equivalent
      c. Inferior
      d. Not assessed
   D. Incidence of ovarian hyperstimulation syndrome (OHSS)
      a. Higher
      b. Equivalent
      c. Lower
      d. I have not compared

11. Which ovarian reserve tests do you primarily rely on for determining individualized gonadotropin dosing?
    a. Anti-Müllerian Hormone (AMH) & Antral Follicle Count (AFC)
    b. Age & BMI
    c. Previous ovarian response
    d. All of the above
12. What is your preferred gonadotropin in conventional IVF?
    a. Recombinant FSH +/- Recombinant LH
    b. Combination of recombinant FSH & HMG
    c. Urinary FSH and HMG
    d. Only HMG
13. What is your preferred starting dose of gonadotropin for a hyper responder patient?
    a. 75 IU
    b. 100 – 200 IU
    c. 225 IU
    d. 300 IU
14. What is your preferred starting dose of gonadotropin for a poor responder patient?
    a. 225 IU
    b. 300 IU
    c. 450 IU
    d. 600 IU
15. Which trigger do you prefer in high responders (e.g., patients with a high risk of OHSS)?
    a. GnRH agonist trigger only
    b. Dual trigger (HCG + GnRH agonist combined.
    c. Standard HCG trigger only
    d. Low dose HCG trigger
16. For patients with a history of suboptimal oocyte maturation, which trigger do you find most effective?
    a. GnRH agonist trigger
    b. Dual trigger
    c. Double trigger
    d. HCG trigger
17. What are the key factors influencing your choice of trigger for final oocyte maturation?
    a. Number of follicles
    b. Serum oestradiol before trigger

c. Oocyte maturation rate in previous cycles
d. All of the above

18. What percentage of women with normal ovarian reserve undergo mild stimulation in your practice?
    a. None
    b. Less than 25%
    c. 25–50%
    d. 51–75%

Ques 19-20 – not applicable if the answer to question 18 is none

19. What factors influence your decision to use mild stimulation protocols?
    a. Cost primarily
    b. Previous poor response with conventional dose
    c. Poor ovarian reserve
    d. I don't use mild stimulation
20. What do you use in cases of Mild stimulation
    a. Oral ovulogens only
    b. Low dose gonadotropins only
    c. Both oral ovulogens and low dose gonadotropins
    d. I don't use mild stimulation
21. How do you rate outcome of mild stimulation protocol in your practise
    a. Lower medication costs
    b. Higher cancellation rates
    c. Better pregnancy rates
    d. I have not compared
22. Do you currently use dual stimulation (follicular and luteal phases) for patients with poor ovarian reserve?
    a. Yes
    b. No
23. How do the outcomes of luteal phase stimulation compare to follicular phase stimulation based on your experience?
    a. Higher oocyte yield
    b. Improved embryo development
    c. Higher clinical pregnancy rate
    d. No significant difference in outcomes

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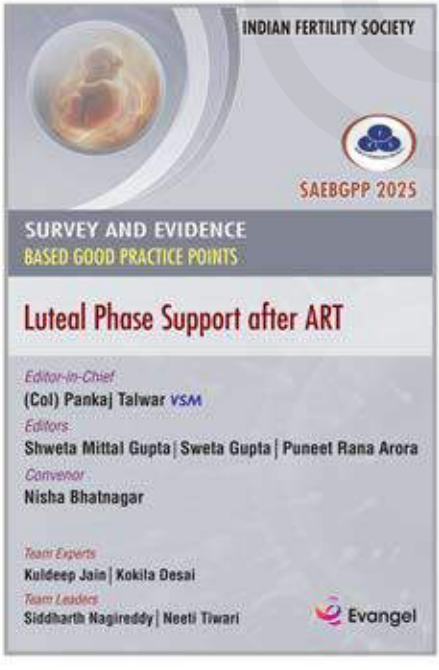
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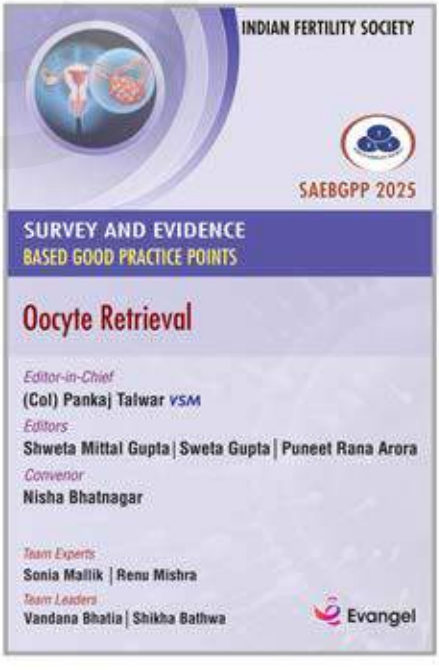
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