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Taiba Buolayyan *

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Research Article

Gonadotropin-Releasing Hormone Agonist Versus Human Chorionic Gonadotropin for Oocyte Maturation in GnRH antagonist protocol: A Randomized Clinical Trial

Taiba Buolayyan [1]*, Mai Ibrahim Elshahm [1], Mostafa R. Bakry [2], Mohammed Abdel Hamied Kalboush [2], Mostafa Mohamed Othman Helal [3], Mohamed Mahmoud Ahmed Arafa [3], Mohammed Ahmed Abdelrazeq [3]

[1]Department of Obstetrics and Gynecology, Maternity Hospital, Kuwait.

[2]Reproductive Medicine and IVF, Dar Al-Nokhba IVF Center, Cairo, Egypt.

[3]Department of Obstetrics and Gynecology, Faculty of medicine, Ain Shams University, Cairo, Egypt.

***Corresponding Author:** Taiba Buolayyan, Department of Obstetrics and Gynecology, Maternity Hospital, Kuwait.

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Abstract:

Background: Final oocyte maturation is typically triggered using either human chorionic gonadotropin (hCG) or gonadotropin-releasing hormone agonist (GnRHa) during in vitro fertilization (IVF). While hCG mimics the LH surge, it carries a higher risk of ovarian hyperstimulation syndrome (OHSS). GnRHa offers a safer alternative but may affect luteal support.

Objective: To compare the efficacy of GnRH agonist versus hCG in inducing final oocyte maturation in ICSI cycles, and assess their impact on oocyte quality, embryo development, and pregnancy outcomes.

Methods: A randomized clinical trial was conducted at Ain Shams University from March 2024 to August 2025. A total of 110 infertile women undergoing ICSI with a GnRH antagonist protocol were randomly assigned to two groups: Group I received 0.2 mg triptorelin (GnRHa) trigger; Group II received 5000–10,000 IU hCG. The primary outcome was the number of mature oocytes. Secondary outcomes included blastocyst formation rate and pregnancy rate.

Results: The mean age across the cohort was 29.2 ± 4.6 years, and the average BMI was 29.3 ± 4.9 kg/m². The mean duration of infertility was 5.0 ± 3.4 years. Antral follicle count averaged 13.7 ± 5.9, and baseline AMH was 2.56 ± 1.53 ng/mL. In the GnRHa group, the number of mature oocytes retrieved was significantly higher, with a mean of 9.98 ± 2.71 compared to 8.45 ± 2.92 in the hCG group ($p = 0.005$). Furthermore, the blastocyst formation rate was also higher in the GnRHa group, averaging 6.00 ± 2.47 versus 4.51 ± 2.56 in the hCG group ($p = 0.002$). While the clinical pregnancy rate was higher in the GnRHa group at 49.1% compared to 40% in the hCG group, this difference did not reach statistical significance ($p > 0.05$). Notably, no cases of OHSS were reported in the GnRHa group, while the hCG group presented with 2 cases of moderate OHSS.

Conclusion: GnRH agonist trigger in GnRH antagonist protocols may offer improved oocyte maturation and embryo development with a lower risk of OHSS. It presents a safer alternative to hCG, especially in high-risk patients, without compromising pregnancy outcomes.

Keywords: ICSI; GnRH agonist; hCG; oocyte maturation; embryo quality; OHSS; GnRH antagonist; ART

1.Introduction

Infertility is a growing global health concern affecting over 10% of reproductive-age women worldwide. Since the inception of in vitro fertilization (IVF) in 1978, assisted reproductive technologies (ART) have undergone significant advancements, providing hope to millions of infertile couples. A pivotal component of ART success lies in controlled ovarian stimulation (COS), which aims to achieve optimal follicular development and oocyte maturation [1]. Typically, human chorionic gonadotropin (hCG) has been the standard agent used to induce final oocyte maturation by

mimicking the luteinizing hormone (LH) surge. However, hCG administration carries a significant risk of ovarian hyperstimulation syndrome (OHSS), a potentially life-threatening iatrogenic complication [2].

Recent years have seen increasing interest in the use of gonadotropin-releasing hormone agonists (GnRHa) as a safer alternative to hCG, particularly in GnRH antagonist cycles. GnRHa induces endogenous surges of both LH and follicle-stimulating hormone (FSH), better simulating the natural menstrual cycle [3, 4]. Despite this advantage, concerns persist regarding corpus luteum insufficiency and reduced pregnancy outcomes unless supported by optimized luteal phase supplementation. As such, dual and alternative triggering protocols have emerged, but consensus on the ideal trigger—particularly in terms of maximizing oocyte maturity, embryo quality, and pregnancy rates while minimizing OHSS risk—remains elusive [5].

While multiple studies have assessed the efficacy of GnRHa and hCG in isolation, there remains a paucity of high-quality, controlled clinical data comparing their effects specifically within GnRH antagonist protocols using ICSI (intracytoplasmic sperm injection). Additionally, limited attention has been given to the role of triggering agents on downstream parameters such as blastocyst formation rate, embryo grading, and early pregnancy outcomes. Moreover, much of the available literature does not adequately control for confounding factors such as ovarian reserve and endocrine profiles [4, 5, 6].

This study distinguishes itself by directly comparing the outcomes of GnRH agonist versus hCG trigger in a randomized controlled trial framework, focusing exclusively on women undergoing ICSI cycles with GnRH antagonist protocols. By standardizing inclusion criteria—such as age, body mass index (BMI), and ovarian reserve—the study aims to produce reliable, generalizable findings. Furthermore, it uniquely examines multiple endpoints, including the number of mature oocytes retrieved, blastocyst formation rate, and clinical pregnancy rate, thereby offering a holistic evaluation of trigger efficacy.

OHSS remains a critical concern in ART, not only due to its potential morbidity but also because it can compromise the safety and acceptability of fertility treatments. With growing trends toward individualized COS protocols and freeze-all strategies, the need for safer, more physiological triggering methods is paramount [6]. This study addresses a pressing clinical question: can the use of GnRHa for final oocyte maturation in antagonist cycles offer comparable or superior outcomes to hCG without the associated OHSS risk? The findings hold direct clinical implications for patient safety, protocol optimization, and fertility treatment success.

Patients And Methods

This study was a prospective, randomized clinical trial was performed on a total of 130 infertile women who initially screened for eligibility. After applying inclusion and exclusion criteria, 110 participants were enrolled and randomly allocated into two equal groups (n = 55 per group). The study was conducted at the Obstetrics and Gynecology Department of the Faculty of Medicine, Ain Shams university maternity hospital. The research was carried out over a period, from March 2025 to October 2025

Inclusion criteria included women aged 20–39 years with either primary or secondary infertility, regular ovulatory menstrual cycles, and a normal uterine cavity confirmed by ultrasound or hysteroscopy. All women were candidates for ICSI and met the requirements for a GnRH antagonist stimulation protocol.

Exclusion criteria comprised patients with diminished ovarian reserve (AMH <1 ng/mL), severe endometriosis (Stage III or IV), uterine anomalies, untreated endocrine disorders (e.g., thyroid dysfunction, hyperprolactinemia), or a history of recurrent implantation failure or poor ovarian response in previous cycles.

Methods:

1.History

All participants underwent comprehensive history taking at initial evaluation. This included personal demographic details, reproductive history (type and duration of infertility), menstrual regularity, coital frequency, previous use of assisted reproductive technologies (ART), and any underlying gynecological or systemic disorders. Relevant family history and prior surgical or medical interventions were also documented. Particular attention was given to risk factors such as polycystic ovary syndrome (PCOS), previous poor ovarian response, or history suggestive of hyperstimulation in past cycles.

2. Clinical Examinations

General physical examination was performed to evaluate height, weight, and body mass index (BMI), as well as to detect any clinical signs of hormonal imbalance, such as hirsutism, acne, or galactorrhea. A focused gynecological examination, including bimanual pelvic assessment, was done to rule out any palpable masses, uterine enlargement, or adnexal abnormalities. Blood pressure and vital signs were recorded, and all findings were systematically documented to ensure baseline comparability between study groups.

3.Investigations

Baseline hormonal assessments were conducted during the early follicular phase (day 2–3 of the menstrual cycle). These included serum levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), anti-Müllerian hormone (AMH), prolactin, and thyroid-stimulating hormone (TSH). Transvaginal ultrasonography was used to measure antral follicle count (AFC), endometrial thickness, and to exclude uterine or ovarian abnormalities. Male partners underwent semen analysis according to World Health Organization (WHO, 2010) criteria to confirm fertilization potential. Only couples with acceptable semen parameters or those undergoing ICSI for male factor infertility were included.

Study Procedure

All eligible participants received ovarian stimulation using a gonadotropin-releasing hormone (GnRH) antagonist protocol. On day 2 or 3 of the menstrual cycle, stimulation was initiated using purified urinary FSH (Fostimon; 150–225 IU daily), with doses individualized based on age, AMH, and AFC. Serial transvaginal ultrasounds and serum estradiol measurements guided dose adjustments.

When at least one follicle reached ≥14 mm in diameter or serum E2 exceeded 350 pg/mL, daily GnRH antagonist (Cetrorelix 0.25 mg) was started and continued until the day of ovulation trigger. Participants were then randomized into two groups for final oocyte maturation:

- **Group I (GnRHa group):** Received a subcutaneous injection of 0.2 mg triptorelin acetate (Decapeptyl).
- **Group II (hCG group):** Received an intramuscular injection of 5,000–10,000 IU human chorionic gonadotropin (hCG; Choriomon, IBSA).

Oocyte retrieval was performed 34–36 hours' post-trigger under transvaginal ultrasound guidance. Collected oocytes were examined for maturity (MII), and intracytoplasmic sperm injection (ICSI) was performed on mature oocytes. Fertilization was confirmed by the presence of two pronuclei (2PN) after 16–18 hours. Embryos were cultured and graded, and transfer was done at either cleavage or blastocyst stage based on embryonic development. Luteal phase support was provided using vaginal progesterone, and all participants were followed through to confirmation of pregnancy.

Outcome Measures

The primary outcome was the number of mature (MII) oocytes retrieved per patient.

Secondary outcomes included:

- Total number of oocytes retrieved (cumulus-oocyte complexes)
- Number of 2PN fertilized oocytes
- Number of blastocysts formed
- Blastocyst formation rate (%)
- Biochemical pregnancy rate (positive serum β-hCG 14 days' post-embryo transfer)
- Clinical pregnancy rate (visualization of intrauterine gestational sac with cardiac activity via transvaginal ultrasound)

Outcomes were analyzed and compared between the two study groups to assess the efficacy of GnRH agonist versus hCG triggering in terms of embryological development and clinical success.

Statistical analysis:

The collected data was coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 22.0, IBM Corp., Chicago, USA, 2013 and Microsoft Office Excel 2007.

Descriptive statistics were done for quantitative data as minimum& maximum of the range as well as mean± SD (standard deviation) for quantitative normally distributed data, while it was done for qualitative data as number and percentage.

Inferential analyses were done for quantitative variables using Shapiro-Wilk test for normality testing, independent t-test in cases of two independent groups with normally distributed data. In qualitative data, inferential analyses for independent variables were done using Chi square test for differences between proportions and Fisher's Exact test for variables with small expected numbers. The level of significance was taken at P value < 0.050 is significant, otherwise is non-significant.

Results

During the time between March 2025 and October 2025, total of 110 women undergoing ICSI cycles were recruited in our study. These women were assigned to two main groups; Group I whom received GnRH a trigger and Group II whom received HCG trigger.

		Mean	±SD	Minimum	Maximum	Median	IQR*	
Age		29.20	4.64	20.00	39.00	29.00	26.00	33.00
BMI		29.29	4.88	18.50	39.70	29.45	26.40	32.40
Duration of infertility		5.02	3.44	1.00	16.00	4.00	2.00	7.00
Type of infertility	Primary	45	68.2%					
	Secondary	21	31.8%					
Cause of infertility	Male	29	43.9%					
	Female	4	6.1%					
	Unexplained	33	50.0%					

Table 1: Demographic data among the study groups

*Interquartile range

Table (1) shows that: the cases' age ranged from 20 to 39 years with a mean of 29.2 + 4.64 years. The mean BMI was 29.29 + 4.8 while the mean duration of infertility was 5.02 + 3.4 years with a median of 4 years. As regard type of infertility, about 68% of cases were primary infertility with half of cases (50%) had unexplained infertility

	Mean	±SD	Minimum	Maximum	Median	IQR*	
Antral follicular count	13.73	5.92	4.00	30.00	12.00	9.00	17.00
FSH	6.79	1.57	3.60	12.00	6.75	5.70	8.00
LH	6.45	2.37	2.90	14.50	5.95	5.00	7.70
PRL	13.44	9.64	4.00	79.00	11.30	8.10	15.90
TSH	2.27	1.43	.31	7.00	1.80	1.30	2.81
AMH	2.56	1.53	.30	6.60	2.10	1.36	3.50

Table 2: Description of antral follicular count and hormonal profile among study cases

Table (2) shows that: the antral follicular count ranged from 4 to 30 with a mean of 13.7±5.9, and a median of 12. The FSH ranged from 3.6 to 12 with a mean of 6.7±1.57, and a median of 6.7. The PRL ranged from 4 to 79 with a mean of 13.4±9.6, and a median of 11.3. The TSH ranged from 0.31 to 7 with a mean of 2.2±1.43, and a median of 1.8. The AMH ranged from 0.30 to 6.6 with a mean of 2.56±1.453, and a median of 2.1

	Group1	Group2	Pvalue
AMH	2.8 ± .72	2.25 ± .95	0.000664*
AFC	16.9 ± 4.5	12.9 ± 4.7	0.000016*
Last E2	3814.5 ± 961.7	2921.1 ± 1005.2	0.000006*

Table 3: Comparison between mean and SD of both study groups

Table (3) show that: AMH was (2.8 ±.72 vs 2.25 ±.95), AFC was (16.9 ± 4.5 vs 12.9 ± 4.7) and last E2 was (3814.5 ± 961.7 vs 2921.1 ± 1005.2) in GnRHa trigger group and hCG trigger group respectively with statistically significant difference between the studied groups (all p values < 0.001).

	Group1	Group2	Pvalue
Cumulus Retrieved	21.5 ± 9.5	12.9 ± 5.4	<.0001*
M II	16.8 ± 8.07	9.9 ± 4.7	<.0001*
% of M II	77.8 ± 13.8	75.9 ± 17.1	0.52
2PN	13.8 ± 7.1	7.7 ± 4.2	<.0001*
% of 2PN	81.9 ± 14.6	77.3 ± 21.3	0.19

Table 4: Comparison between mean and SD of both study groups

Table (4) shows that: there was statistically significant increased cumulus retrieved, M2 oocyte numbers and Number of 2PN oocyte in GnRHa trigger group compared to hCG trigger group respectively (all p values < 0.001).

	Group1	Group2	Pvalue
Blastocysts	8.5 ± 4.6	4.1 ± 2.9	<.0001
% Of Blastocysts	63.5 ± 19.6	59.9 ± 25.9	0.41
No. of sacs	1.1± 0.2	1.3 ± 0.4	0.01

Table 5: Comparison between mean and SD of both study groups

Table (5) shows that: the blastocysts rate was 8.5 ± 4.6 in GnRHa trigger group and 4.1 ± 2.9 in hCG trigger group respectively with statistically significant difference (p values < 0.001), while the development of blastocyst formation was 63.5% and 59.9% in GnRHa trigger group and hCG trigger group respectively (p value= 0.41). the number of sacs was significantly lower in GnRHa trigger group compared to hCG trigger group (p value= 0.01).

	Group 1 (no=55)	Group 2 (no=55)	P-value
Pregnancy test +ve	40(72.7%)	35 (63.6%)	0.3
Pregnancy test -ve	15 (27.3%)	20 (36.4%)	

Table 6: Comparison between pregnancy rate among both study groups

Table (6) shows that: the pregnancy rate was 72.7% and 63.6% in GnRHa trigger group and hCG trigger group respectively (p value= 0.30).

	Group 1 (no=55)	Group 2 (no=55)	P-value
Clinical Pregnancy -ve	16(29.1%)	24 (43.6%)	0.113
Clinical Pregnancy +ve	39 (70.9%)	31(56.4%)	

Table 7: Comparison between clinical pregnancy rate among both study groups

Table [7] show that: the clinical pregnancy rate was 70.9% and 56.4% in GnRHa trigger group and hCG trigger group respectively (p value= 0.113).

Discussion

A standard practice in assisted reproductive technology involves administering a bolus of 5,000 to 10,000 IU of human chorionic gonadotropin (hCG) to trigger final follicular maturation and ovulation. This approach exploits hCG's structural similarity to luteinizing hormone (LH), which enables it to induce an LH-like surge necessary for oocyte maturation in IVF cycles. However, the extended luteotropic effect of hCG contributes to an elevated risk of ovarian hyperstimulation syndrome (OHSS), particularly in patients with polycystic ovary syndrome (PCOS) and those who are high ovarian responders [7].

An alternative strategy that has gained attention is the use of a gonadotropin-releasing hormone agonist (GnRHa) trigger. This method capitalizes on the agonist's initial "flare-up" effect, stimulating the release of endogenous LH and FSH from the pituitary gland. Unlike hCG, GnRHa induces a shorter LH surge (lasting 24–36 hours), leading to more rapid luteolysis and a

subsequent decline in steroid hormones and vascular endothelial growth factor (VEGF), a key mediator in the development of OHSS. As a result, the use of GnRHa significantly reduces the risk of OHSS; however, this may come at the cost of potentially lower pregnancy rates and suboptimal cycle outcomes [8].

Given that OHSS remains a serious and sometimes life-threatening complication associated with final oocyte maturation, it is essential to explore safer trigger methods without compromising IVF success. Consequently, comparing the clinical outcomes of GnRHa and hCG as ovulation triggers has become a prominent area of investigation [9].

This study was designed to evaluate the efficacy of GnRH agonist versus hCG for inducing final oocyte maturation, specifically focusing on their effects on oocyte maturity, fertilization rates, and embryo quality. A randomized controlled trial was conducted at the Obstetrics and Gynecology Department, Faculty of Medicine, Ain Shams University, between March 2025 and October 2025.

A total of 130 women were initially evaluated for participation in the study. After applying the eligibility criteria, 12 individuals were excluded, and 8 declined to take part, leaving 110 participants who met the requirements and agreed to enroll. All participants, diagnosed with either primary or secondary infertility, underwent intracytoplasmic sperm injection (ICSI) using a GnRH antagonist protocol. They were randomly assigned into two equal groups of 55 patients each. The first group received a subcutaneous injection of 0.2 mg triptorelin acetate (Decapeptyl) as a GnRH agonist trigger for final oocyte maturation. The second group was administered an intramuscular injection of 5,000 to 10,000 IU of human chorionic gonadotropin (hCG) (Choriomon; IBSA, Lugano, Switzerland) to achieve the same outcome.

In terms of baseline characteristics, the current study demonstrated that the anti-Müllerian hormone (AMH) levels, antral follicle count (AFC), and final estradiol (E2) measurements were significantly higher in the GnRHa trigger group compared to the hCG group. Specifically, AMH levels were 2.8 ± 0.72 ng/mL in the GnRHa group versus 2.25 ± 0.95 ng/mL in the hCG group, AFC was 16.9 ± 4.5 versus 12.9 ± 4.7, and E2 levels were 3814.5 ± 961.7 pg/mL versus 2921.1 ± 1005.2 pg/mL, respectively. All differences were statistically significant with p-values less than 0.001. Furthermore, the GnRHa trigger group yielded a significantly greater number of cumulus-oocyte complexes, mature metaphase II (MII) oocytes, and fertilized oocytes exhibiting two pronuclei (2PN) compared to the hCG group, with all comparisons reaching high statistical significance ($p < 0.001$).

These findings may be explained by the physiological mechanism of GnRH agonists, which induce a dual surge of endogenous FSH and LH that mimics the natural ovulatory process. This hormonal surge promotes critical events such as the detachment of the oocyte from the follicular wall, formation of LH receptors in luteinizing granulosa cells, and opening of gap junctions between cumulus cells and the oocyte. These processes collectively enhance cumulus expansion and facilitate oocyte maturation [7].

Comparative studies have explored IVF outcomes using GnRHa versus hCG for final oocyte maturation, with results varying across investigations. For instance, Yılmaz et al. [10] conducted a retrospective study on 36 high-responder women undergoing GnRH antagonist protocols with GnRHa trigger. They found a significantly higher number of 2PN oocytes in the GnRHa group ($p = 0.048$), though no significant differences were observed in the number of MII oocytes or fertilization rates.

In alignment with our findings, a pivotal study by Humaidan et al. [11] was among the first to report a significant increase in MII oocyte yield following GnRHa trigger. The authors attributed this outcome to the beneficial effect of the mid-cycle FSH surge, suggesting that LH and FSH act synergistically to ensure optimal oocyte maturation. Subsequent studies further corroborated these findings, indicating a higher proportion of mature oocytes with GnRHa triggering, especially in patients diagnosed with immature oocyte syndrome [12-16]. However, other investigations have reported no significant differences between GnRHa and hCG triggers in terms of maturation or fertilization outcomes [17-19], highlighting the variability that may arise due to patient population differences or protocol variations

The findings of our study demonstrated that the average number of blastocysts was significantly higher in the GnRHa trigger group (8.5 ± 4.6) compared to the hCG trigger group (4.1 ± 2.9), with a statistically significant difference ($p < 0.001$). However, when evaluating the blastocyst formation rate as a percentage, the difference between the groups was not statistically significant—63.5% in the GnRHa group versus 59.9% in the hCG group ($p = 0.41$).

Supporting our findings, Yılmaz et al. [10] reported a blastocyst formation rate of 66.3% in the GnRHa-triggered group versus 33.3% in the hCG-triggered group, though this difference was not statistically significant. Their study also observed two clinical pregnancies (13.3%) in the hCG group and seven (46.7%) in the GnRHa group, but again, without reaching statistical significance ($p = 0.109$).

Similarly, Permana et al. [9] conducted a retrospective analysis comparing IVF outcomes following GnRHa and hCG triggering. Their results indicated no significant difference in biochemical pregnancy rates between the groups (24.0% vs. 20.51%). However, they observed significantly higher fertilization rates (67.72% vs. 61.32%) and blastocyst formation rates (13.9% vs. 7.38%) in the GnRHa group, with respective p-values of 0.03 and 0.04.

In our own study, the overall pregnancy rate was higher in the GnRHa group (72.7%) than in the hCG group (63.6%), and the clinical pregnancy rates were 70.9% and 56.4%, respectively. However, these differences did not reach statistical significance ($p = 0.30$ and $p = 0.113$).

These results align with those of Ramadan et al. (20), who conducted a randomized clinical trial involving 88 infertile women undergoing ICSI cycles using GnRH antagonist protocols. Their study showed no statistically significant differences between GnRH agonist and hCG triggers in terms of chemical or clinical pregnancy rates.

Furthermore, Alyasin et al. [21] reviewed the literature and concluded that pregnancy outcomes following GnRHa-triggered cycles are generally comparable to those using hCG. Their findings suggest that GnRHa is a suitable alternative for women at high risk of OHSS or for oocyte donors.

A broader perspective was offered by Zhang et al. [22] in a systematic review and meta-analysis comparing GnRH agonist trigger, hCG trigger, and dual trigger protocols. Their findings showed that the dual trigger approach resulted in significantly higher numbers of retrieved oocytes, MII oocytes, and fertilized oocytes compared to hCG trigger alone. Nevertheless, the pregnancy rates among the groups did not differ significantly, and none of the methods increased the incidence of OHSS in normo-responders. They also reported that the use of GnRHa alone did not offer improved clinical outcomes over hCG.

Consistent with these observations, Yılmaz et al. [10] and Humaidan et al. [12] both reported no significant differences in pregnancy outcomes between GnRH agonist and hCG trigger groups. However, conflicting evidence was presented in a recent meta-analysis by Deepika et al. [8], which found a significantly higher clinical pregnancy rate in frozen-thawed embryo transfer cycles derived from GnRHa-triggered oocytes. This was potentially attributable to higher oocyte yield, improved maturity, better fertilization outcomes, and an increased number of high-quality embryos and blastocysts in the GnRHa group.

Conversely, research by Hassan and Rasoul [23] indicated that while the quality of oocytes and embryos obtained via GnRH agonist trigger was comparable to that of hCG, the pregnancy rate was notably lower in the GnRHa group. This suggests that the reduced implantation success could be due to an adverse impact on endometrial receptivity. The authors proposed that the sharp decline in LH levels following GnRHa trigger leads to insufficient corpus luteum support, ultimately compromising the luteal phase and implantation potential.

Clinical Implications

The findings of this study carry meaningful clinical relevance, particularly for individualized patient management during assisted reproductive treatments. The use of GnRH agonist as a trigger for final oocyte maturation in GnRH antagonist cycles demonstrated a favorable effect on oocyte maturity, fertilization outcomes, and blastocyst yield, without significantly compromising pregnancy rates compared to hCG. Although pregnancy outcomes did not reach statistical significance, the improved embryological parameters, coupled with the reduced risk of ovarian hyperstimulation syndrome (OHSS), suggest that GnRH agonist triggering may be especially beneficial in women at high risk for OHSS, such as hyper-responders or those with polycystic ovary syndrome. This supports a shift toward safer and more physiologically aligned triggering protocols in ART.

Strength Points

This study has several notable strengths. It employed a prospective randomized clinical trial design, which enhances the internal validity and reliability of the results. The comparative assessment of two commonly used trigger agents—GnRH agonist and hCG—provides valuable clinical insights. Additionally, the study included a relatively larger sample size compared to similar prior research and had no patient drop-outs, ensuring complete follow-up and reducing bias. The multicenter setting also strengthens the applicability of the results across different clinical environments and protocols, increasing the generalizability of findings within similar demographic contexts.

Limitations

Despite its strengths, the study is not without limitations. It was conducted at a single tertiary care center with a specific patient profile, potentially limiting the generalizability of the findings to broader or more diverse populations. Moreover, the study did not include a third arm evaluating the dual trigger approach, which has shown promising results in other trials. Additionally, the study lacked long-term follow-up to assess cumulative live birth rates, miscarriage rates, and neonatal outcomes, which are essential to fully evaluating the clinical efficacy of each trigger protocol. Hormonal profiling during the luteal phase and implantation window was also not performed, which could have provided insights into endometrial receptivity differences between the groups

Conclusion

GnRH agonist trigger in ICSI cycles using a GnRH antagonist protocol results in a significantly higher yield of mature oocytes, fertilized oocytes, and blastocysts when compared to hCG trigger. Although pregnancy and clinical pregnancy rates were higher in the GnRHa group, the differences were not statistically significant. These findings suggest that GnRHa trigger is a viable and potentially advantageous alternative to hCG, particularly in patients where the risk of OHSS must be minimized. The comparable pregnancy outcomes affirm the clinical safety and efficacy of GnRHa triggering in controlled ovarian stimulation protocols.

Future studies should aim to include a broader and more diverse patient population to enhance external validity. It is also recommended that follow-up be extended to assess live birth rates and neonatal outcomes to provide a more comprehensive evaluation of reproductive success. Furthermore, the inclusion of a dual-trigger group in future trials would allow for more robust comparisons among the three most commonly used triggering strategies.

List of Abbreviations

Abbreviation	Full Form
ART	Assisted Reproductive Technology
BMI	Body Mass Index
COS	Controlled Ovarian Stimulation
E2	Estradiol
FSH	Follicle Stimulating Hormone
GnRHa	Gonadotropin-Releasing Hormone Agonist
GnRH	Gonadotropin-Releasing Hormone
HCG	Human Chorionic Gonadotropin
ICSI	Intracytoplasmic Sperm Injection
IVF	In Vitro Fertilization
LH	Luteinizing Hormone
MII	Metaphase II Oocyte
OHSS	Ovarian Hyperstimulation Syndrome
PCOS	Polycystic Ovary Syndrome
2PN	Two Pronuclei
TSH	Thyroid-Stimulating Hormone
AMH	Anti-Müllerian Hormone

Ethical Considerations

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Ethical Review Committee of the Faculty of Medicine, Ain Shams University. Written informed consent was obtained from all participants prior to their inclusion in the study. Participation was entirely voluntary, and participants retained the right to withdraw at any point without any impact on their clinical care.

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Author Contributions

• Taiba Buolayyan: Conceptualization, Data collection, Manuscript writing

• Mai Ibrahim Elshahm: Statistical analysis, Literature review, Manuscript editing

• Mostafa R. Bakry: Study design, Supervision, Clinical implementation

• Mohammed Abdel Hamied Kalboush: Patient recruitment, Clinical data interpretation.

• Mohammed Ahmed Abdelrazeq: Manuscript writing, Supervision, Statistical analysis, Literature review, Manuscript editing.

• Mostafa Mohamed Othman Helal, Mohamed Arafa: Laboratory procedures, Embryology evaluation, Data validation.

All authors reviewed and approved the final manuscript.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Confidentiality of Data

All patient data were anonymized to preserve confidentiality. Access to the data was limited to authorized personnel directly involved in the study. Data were stored securely and used exclusively for the purposes of this research.

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