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Research Article

Impact of Trigger-to-Insemination Interval on Intrauterine Insemination Outcomes: A Retrospective Cohort Study

Puvithra Thanikachalam[1], Gayatri Ravikuppan[2]*, Vedha Sruthi[2], and Sowbarnika Arunkumar[3]

[1]Associate Professor & Senior Consultant, Department of Reproductive Medicine & Obstetrics & Gynaecology, Chettinad Academy of Research and Education, Chennai, India
[2]Postgraduate student, M.Sc Clinical Embryology II year, Chettinad Fertility Services, Department of Reproductive Medicine and Andrology, Chettinad Academy of Research and Education, Chennai, India
[3]Senior Clinical Embryologist, Chettinad Fertility Services, Department of Reproductive Medicine and Andrology, Chettinad Academy of Research and Education, Chennai, India

Abstract

Objective: To assess the Intrauterine Insemination (IUI) outcome based on different time intervals between ovulation trigger and IUI.

Methods: This study presents a retrospective review of 209 patients who received IUI at an Assisted Reproductive Technology (ART) Clinic affiliated with Chettinad Super Speciality Hospital between 2013 and 2024. Couples with unexplained infertility, male partner aged 23-40 years and female partner aged 21-35 years with bilateral patent fallopian tubes were included in the study. The exclusion criteria were abnormal semen parameters, incomplete & frozen samples, double IUI and donor samples. The study cohort was divided into three subgroups based on the time interval between hCG trigger administration and IUI [Group I: Concurrent IUI with hCG trigger (n = 13), Group II: IUI performed at 24 hours following hCG trigger (n = 25), Group III: IUI performed at 36 hours following hCG trigger (n = 171)]. Statistical analysis was performed using IBM SPSS software, with categorical data evaluated by Chi-square test.

Results: Based on the different time interval groups, the clinical pregnancy rate was 7.69 % in Group I, 8% in Group II and 15.2% in Group III. There is no statistical significance between the different time interval of IUI and hCG trigger on IUI outcome (p=0.499).

Conclusion: According to our study, we could not find any correlation between the time interval of IUI and hCG trigger on IUI outcome.

Keywords: intrauterine insemination, ovulation trigger, human chorionic gonadotropin, clinical pregnancy rate

Corresponding Author: Gayatri Ravikuppan; email: gayuravi1904@gmail.com

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1. Introduction

Despite the numerous recent advancements in the Assisted Reproductive Techniques, Intrauterine Insemination (IUI) still remains a recommended treatment option for subfertile couples with unexplained or moderate male factor infertility. [1] IUI with ovarian stimulation has been shown to be more effective than natural cycle IUI, especially in unexplained infertility. Ovarian stimulation with clomiphene citrate or letrozole has provided similar results in most available literature. Ovarian stimulation is usually combined with administration of an ovulation trigger in the form of human Chorionic Gonadotropin (hCG) injections, to eliminate the probability of an unruptured follicle and more importantly to time the IUI procedure.

The success of an IUI cycle is influenced by several key factors, including the age of female partner, duration of infertility, total motile spermatozoa count and number of dominant follicles. [2, 3] IUI is more likely to be successful under the following conditions: a) age of female partner under 30 years, b) duration of infertility less than 2 years c) no other underlying conditions. [4, 5]

Standard practice involves performing IUI between 32 to 36 hours following the ovulation trigger. [6] However, the optimal timing between the ovulation trigger and the IUI procedure remains a topic of debate. The brief window of viability of spermatozoa in the female reproductive tract (48 – 72 hours) and the oocyte post-ovulation (12 – 24 hours) emphasizes the importance of accurately synchronizing IUI with the ovulation trigger to maximize success of fertilization. [7, 8]

Studies indicate that performing an IUI anytime between 0 and 36 hours after hCG trigger administration has no substantial effect on pregnancy rates. [9] Similarly, performing IUI concurrently with hCG trigger administration yields similar pregnancy rate as IUI performed at various time intervals. [10] This is attributed to the fact that the spermatozoa remain viable for upto 72 hours in the female reproductive system, allowing them to be available for fertilization when the oocyte is ovulated.

This study aimed to investigate the optimal time for performing IUI post ovulation trigger administration in order to achieve better pregnancy rates.

2. Materials and Methods

It is a retrospective cohort study in which we analyzed 209 case records of patients who underwent IUI in the Department of Reproductive Medicine & Andrology (ART Clinic affiliated to a tertiary care centre and university teaching hospital), Chettinad Super Speciality Hospital between 2013 and 2024 after obtaining approval from the Institutional Human Ethics Committee, Chettinad Academy of Research & Education (IHEC-I/3204/24).

The couples with unexplained infertility were chosen for the study, including only those with bilateral patent fallopian tubes, female partner aged 21 to 35 years and male partner aged 23 to 40 years. The other criteria for inclusion in the study were when single IUI was done using fresh/neat semen sample collected by masturbation and when the male partner provided complete semen sample.

2.1. Methodology

Women underwent ovarian stimulation with Clomiphene citrate or letrozole from day 2/3 of the cycle for 5 days and follicular growth was monitored using transvaginal ultrasonogram. The cycle was cancelled if more than two dominant follicles developed. hCG trigger was given when the lead follicle measured between 20 – 22 mm in diameter. Either urinary or recombinant hCG preparations were used as ovulation trigger since studies have demonstrated that both the preparations are equally effective and provides similar pregnancy rates. The timing of IUI post hCG trigger was based on various factors like size of follicle, impending changes in endometrium or availability of the male partner.

The study cohort was divided into three subgroups based on the time interval between hCG trigger administration and IUI**:**

Group 1: Concurrent IUI with hCG trigger

Group 2: IUI performed at 24 hours following hCG trigger

Group 3: IUI performed at 36 hours following hCG trigger

The outcome of IUI (clinical pregnancy rate) was correlated with the different time intervals between hCG trigger and IUI. Statistical analysis was performed using IBM SPSS Statistics 30.0.0.0, with categorical data evaluated by Chi-square test. The significance for the variables was set at p value < 0.05.

3. Results

The distribution of study participants based on the timing of IUI relative to hCG trigger administration is illustrated in Figure **1**.

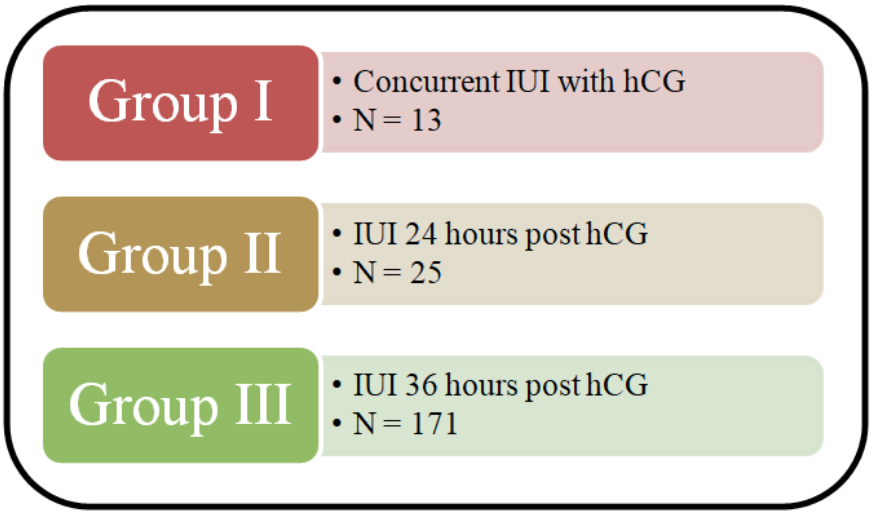

Figure 1: Distribution of study population based on time interval between the hCG trigger and IUI.

Crucial factors that determine the success rates of IUI, like age of the female partner and post-wash semen sample were comparable (Table **1**).

Table 1: Comparison of basic characteristics between the study groups.

	Group I	Group II	Group III	P value
Female Age (yrs)	29.92±2.7	28.2±3.0	28.38±3.2	0.213
Sperm Concentration (million/ml)	44.15±14.3	45.36±28.8	46.23±20.9	0.935
Total Motility (%)	61.31±8.5	61.88±7.5	60.46±9.3	0.74
Post-wash Total Motile Sperm Concentration (million/ml)	43.15±13.3	43.76±31.5	37.67±19.7	0.299

The overall success rate of IUI cycles was 14% (Figure **2**). The clinical pregnancy rate was 7.69% in Group I (concurrent IUI with hCG trigger), 8% in Group II (IUI performed at 24 hours following hCG trigger) and 15.2% in Group III (IUI performed at 36 hours following hCG trigger). However, the differences in pregnancy rates among the groups were not statistically significant (p = 0.499), indicating no significant impact of the time interval between hCG administration and IUI on clinical outcomes (Table **2**).

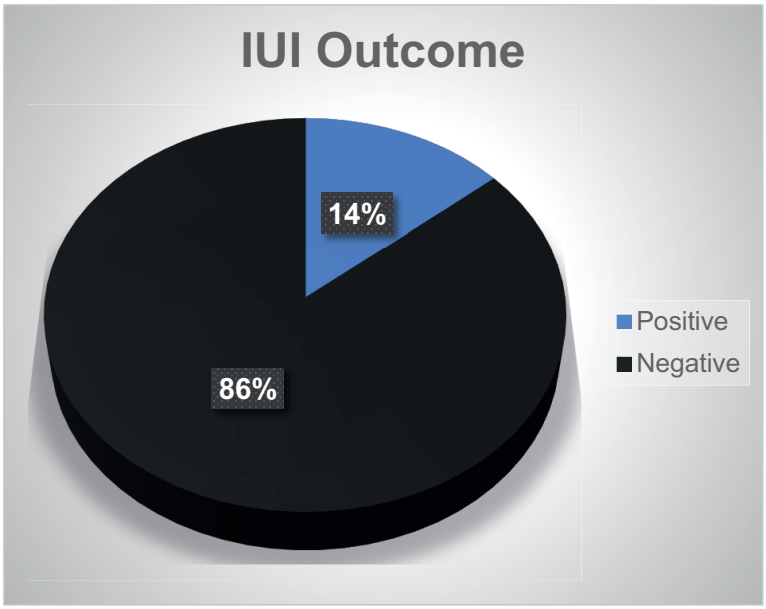

Figure 2: IUI outcome in the overall study population.

Table 2: IUI outcome in the groups based on different time intervals.

Groups	Clinical pregnancy		Statistical Difference
	Numbers	Percentage	
I: Concurrent IUI with hCG (n=13)	1	7.69%	Pearson Chi-Square p-value: 0.499
II: IUI 24 hrs post hCG (n=25)	2	8%	
III: IUI 36 hrs post hCG (n=171)	26	15.2%	

4. Discussion

While international literature reports an average success rate of approximately 9-11% for IUI, [2, 3] our study achieved a mean clinical pregnancy rate of 13.88%. In couples with unexplained infertility, we perform a single IUI subsequent to ovulation induction with oral ovulogens followed by hCG trigger, as per ASRM practice committee recommendations. [9] Among the factors influencing IUI success, this study focuses on analyzing the effect of the timing between hCG trigger and IUI on the outcome of IUI. According to a Cochrane review, [11] the timing of IUI between 24 and 48 hours post hCG trigger administration does not significantly impact pregnancy rates which was in concordance with many other authors who reported no significant difference in the IUI outcome between the two different time intervals. [12, 13]

Studies have compared simultaneous IUI with ovulation trigger and IUI performed at 34 – 36 hours following ovulation trigger and found that the clinical pregnancy rates were comparable among the groups, with no notable differences observed. [14] Even though the clinical pregnancy rates were higher in the group where IUI was done 36 hours post-trigger, the results were not statistically significant. On the other hand, there are conflicting results reporting a higher incidence of pregnancy when IUI was carried out immediately after the hCG trigger administration when compared to the outcome when IUI was performed at 24 – 32 hours following hCG trigger administration. [15]

This may be due to the shorter life-span of oocyte and longer life-span of spermatozoa in the female reproductive tract making it imperative for spermatozoa to be available for the oocyte during this time period to increase the chance of sperm oocyte interaction.

Many studies have concluded that there was a higher pregnancy rate achieved when IUI was done before 40 hours post hCG trigger administration.[16] Despite lack of statistical significance in our study, IUI performed 36 hours post-ovulation trigger yielded a higher clinical pregnancy rate compared to other time intervals. While some authors suggest delaying IUI by 48 hours to optimize endometrial development without compromising oocyte quality, [17, 18] our institution's protocol involves performing IUI within 36 hours post hCG trigger prioritizing timely insemination to preserve oocyte viability in the female reproductive tract.

The study's execution demonstrates significant strengths, particularly in the selection of a population without conflicts of interest and the implementation of measures to rule out bias, ultimately yielding high-quality and trustworthy results. One major limitation of this study is its sample size and single centre design. Further studies can be done with a larger sample size to provide more insight.

5. Conclusion

According to our study, we could not find any correlation between the time interval of IUI and hCG trigger on IUI outcome. Therefore, IUI can be scheduled at any time between 0 to 36 hours after hCG trigger

administration prioritizing timely insemination to preserve oocyte viability in the female reproductive tract. The reason behind achieving similar pregnancy rates in different time intervals can be due to the shorter viability of oocyte and the availability of spermatozoa around the time of ovulation and longer viability of spermatozoa in the female reproductive tract which provides a higher chance of fertilization post-ovulation.

Declarations

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Nil

Conflicts of Interest

Nil

Ethical Approval

Approval obtained from the Institutional Human Ethics Committee, Chettinad Academy of Research & Education (IHEC-I/3204/24).

Data Availability Statement

The clinical data of this article is available upon reasonable request to the corresponding author.

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