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# Effect of dual trigger with chorionic gonadotropin hormone and follicle-stimulating hormone on endometrial thickness in infertile women who had superovulation with an aromatase inhibitor

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**Keyword**
Dual trigger, Beta HCG, Endometrial thickness, Infertility, an Aromatase inhibitor.

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## Abstract:

Beginning in October 2020 and ending in April 2021, researchers from Al-Nahrain University's High Institute for Infertility Diagnosis and Assisted Reproductive Technologies compared the success rates of two different methods of diagnosing and treating infertility. The major purpose of the research was to assess the impact of a combined trigger (follicle-stimulating hormone [FSH] and human chorionic gonadotropin [hCG]) on endometrial receptivity (endometrial thickness, endometrial pattern, sub-endometrial blood flow). A total of 100 females took part in the study. All patients gave their informed written consent, and the study was approved by the Al-Nahrain University Ethics Committee. Procedure Time To confirm ovulation, measure and analyze the endometrial pattern, and examine the sub-endometrial blood flow, a vaginal ultrasound was done 36 to 48 hours following trigger

ovulation. All four hormones (FSH, LH, Progesterone, and E2) were tested in the blood at the same time to determine whether a couple was fertile, a complete medical history, and physical examination whereas performed on each member of the pair. An ultrasound vaginal probe was used to do the transvaginal examination. Patients were placed in the dorsal lithotomy position with an empty bladder for early follicular US (CD 2-3) to assess the number of antral follicles, measure endometrial thickness, and rule out ovarian cysts or other pathology. A second ultrasound was performed during the middle of the cycle (CD9-14) to determine whether a mature follicle had been found. A multiplanar image of the uterus was acquired after an ultrasound scan was swept across the mid-sagittal plane. Endometrial thickness in the median longitudinal plane of the uterus was calculated as the largest distance from one basal endometrial interface via the endometrial canal to the opposite endometrial-myometrial interface of the anterior-posterior uterine wall. A statistically significant difference was found between Group A's average E2 concentration of 69.62 pg/mL and Groups B and C's concentrations of 53.32 and 36.65 pg/mL. (P 0.001). In group C, there was a statistically significant difference in E2 levels on the day of the trigger and the day of the IUI (P = 0.036). On the day of IUI compared to the day of trigger, no statistically significant differences were seen between the study groups for any of the other hormonal indicators (P > 0.05). There were no significant differences (P > 0.05) in any of the baseline clinical measures between the research groups. All clinical indicators were comparable across groups (P > 0.05). There were no statistically significant differences (P > 0.05) between the research groups on any other clinical indicators. When comparing groups, A, B, and C on the decline in RI between the trigger and IUI days, group A significantly outperformed the others (P = 0.003). There was no statistically significant difference (P > 0.05) in any of the other clinical parameters between the IUI and trigger groups on the day of IUI.

**Keywords:** Dual trigger, Beta HCG, Endometrial thickness, Infertility, an Aromatase inhibitor.

# تأثير الزناد المزدوج مع هرمون موجهة الغدد التناسلية المشيمية والهرمون المنبه للجريب على سمك بطانة الرحم لدى النساء المصابات بالعقم اللائي لديهن إباضة مفرطة مع مثبطات أروماتيز

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## الخلاصة:

بدءًا من أكتوبر ٢٠٢٠ وانتهى في أبريل ٢٠٢١ ، قارن باحثون من المعهد العالي لتشخيص العقم والتقنيات المساعدة على الإنجاب في جامعة النهرين معدلات نجاح طريقتين مختلفتين لتشخيص وعلاج العقم. كان الغرض الرئيسي من البحث هو تقييم تأثير المحفز المركب (الهرمون المنبه للجريب [FSH] والغدد التناسلية المشيمية البشرية [HCG]) على تقبل بطانة الرحم (سمك بطانة الرحم ، نمط بطانة الرحم ، تدفق الدم تحت بطانة الرحم). شارك في الدراسة مجموع ١٠٠ أنثى. أعطى جميع المرضى موافقتهم الخطية المستنيرة ، وتمت الموافقة على الدراسة من قبل لجنة الأخلاقيات بجامعة النهرين. وقت الإجراء لتأكيد الإباضة وقياس وتحليل نمط بطانة الرحم وفحص تدفق الدم تحت بطانة الرحم ، تم إجراء الموجات فوق الصوتية المهبلية بعد ٣٦ إلى ٤٨ ساعة من بدء الإباضة. تم اختبار الهرمونات الأربعة (FSH وLH وPROGESTERONE وE٢) في الدم في نفس الوقت. من أجل تحديد ما إذا كان الزوجان يتمتعان بالخصوبة أم لا ، تم إجراء تاريخ طبي كامل وفحص جسدي لكل فرد من الزوجين. تم استخدام مسبار الموجات فوق الصوتية المهبلي لإجراء الفحص المهبلي. تم وضع المرضى في وضع استئصال الحصاة الظهرية مع وجود مثانة فارغه مع فحص الجريبات في جهاز الموجات فوق الصوتية(CD 2-3) لتقييم عدد البصيلات الغارية ، وقياس سمك بطانة الرحم ، واستبعاد أكياس المبيض أو غيرها من الأمراض. تم إجراء الموجات فوق الصوتية الثانية خلال منتصف الدورة (CD9-14) لتحديد ما إذا كان قد تم العثور على جريب ناضج أم لا. تم العثور على فرق معتد به إحصائيًا بين متوسط تركيز E2 للمجموعة A البالغ ٦٩,٦٢ بيكوغرام / مل وبين تركيزات المجموعتين B وC البالغة ٥٣,٣٢ و ٣٦,٦٥ بيكوغرام / مل. (ص ٠,٠٠١). في المجموعة C ، كان هناك فرق ذو دلالة إحصائية في مستويات E2 في يوم المشغل ويوم IUI (P = 0.036). في يوم IUI مقارنة بيوم التحفيز، لم تُلاحظ فروق ذات دلالة إحصائية بين مجموعات الدراسة لأي من المؤشرات الهرمونية الأخرى (P> 0.05). لم تكن هناك فروق ذات دلالة إحصائية (P> 0.05) في أي من التدابير السريرية الأساسية بين مجموعات البحث. كانت جميع المؤشرات السريرية قابلة للمقارنة عبر المجموعات (P> 0.05). لا توجد فروق ذات دلالة إحصائية (P> 0.05) بين مجموعات البحث على أي مؤشرات سريرية أخرى. عند مقارنة المجموعات A وB وC عند الانخفاض في RI بين أيام التحفيز وأيام IUI ، تفوقت المجموعة A بشكل كبير على المجموعات الأخرى (P = 0.003). لم يكن هناك فرق ذو دلالة إحصائية (P> 0.05) في أي من المعلمات السريرية الأخرى بين IUI ومجموعات التحفيز في يوم IUI.

**الكلمات المفتاحية:** التحفيز المزدوج. HCG بيتا ؛ سمك بطانة الرحم العقم. مثبط أروماتيز.

## 1. INTRODUCTION:

Despite merely providing exposure equivalent to LH, HCG is an effective oocyte maturation inducer, indicating that the mid-cycle FSH surge ordinarily present in the natural cycle is not necessary for successful oocyte maturation. Comparing the benefits of GnRHa and kisspeptin to those of hCG and rLH, one is that they may promote the concurrent synthesis of FSH as well as LH-like activity. FSH may promote nuclear tissue maturation, cumulus expansion, and the synthesis of LH receptors in luteinizing granulosa cells [1]. Positive and negative feedback mechanisms are responsible for the regulation of the ovulatory cycle. The pattern of secretion of kisspeptin, gonadotrophin-releasing hormone (GnRH), follicle-stimulating hormone (FSH), and luteinizing hormone (LH) is regulated by steroid sex hormones generated by the ovaries. These hormones in turn affect how ovarian hormones are released. The rupture and release of the dominant follicle from the ovary into the fallopian tube, where it has the potential to be fertilized, is what is known as ovulation. Ovulation is a physiological process. Ovulation is the process through which the dominant follicle is discharged into the fallopian tube. Throughout the ovulation process, the gonadotropic hormones (FSH and LH) are what regulate when an egg is released [2]. The consequences of a midcycle increase in FSH include induction of plasminogen activity, promotion of LH receptor synthesis in luteinizing granulosa cells, nuclear maturation, and cumulus expansion. Research conducted on animals has demonstrated that FSH is capable of stimulating ovulation. Ovulation was produced in hypophysectomized rats using LH-free recombinant FSH, and as a result, a dose-dependent ovulation rate of one hundred percent was achieved [3]. The follicle-stimulating hormone also contributes to the preservation of open gap junctions between the cumulus cells and the oocyte. This hormone may thus be essential to the signaling cascades [4]. It is believed that FSH collaborates with other hormones to set the stage for ovulation to occur once an egg has fully matured [2]. An intrauterine insemination is a treatment option for couples with moderate to severe male factor infertility when the female spouse has at least one intact tube. The effectiveness of this kind of assisted reproduction is limited by several parameters, which have been the subject of decades' worth of study. Semen quality, female etiology, synchronization with ovulation, evaluation of follicle rupture, number of inseminations each cycle, and the impact of uterine contractions are some of these criteria. These elements must be present for a good result. When all other factors are considered, satisfactory outcomes can be achieved using intrauterine insemination, which is a method that is both less intrusive and less expensive than in vitro fertilization [5]. To evaluate if endometrial receptivity indicators might be enhanced by

using a dual trigger (FSH and hCG) (endometrial thickness, endometrial pattern, sub-endometrial blood flow).

## 2. Materials and Methods

A prospective comparative study was conducted at the High Institute for Infertility Diagnosis and Assisted Reproductive Technologies, Al-Nahrain University, from October 2020 to April 2021. A hundred women were included in this study. Every patient gave her written informed consent before taking part in the study, which was approved by the Ethics Committee, Al-Nahrain University. One hundred and one women were recruited from the patient population of the consultant clinic at the High Institute for Infertility Diagnosis and Assisted Reproductive Technologies for this research.

Exclusion criteria: All medical disorders that are incompatible with pregnancy, such as endometriosis, ovarian cysts, bilateral tubal obstructions, and acute genital tract infection in either parent or others, are prohibited.

### Methods.

All The women who participated in the research were asked detailed questions about their obstetrical and gynecological histories, as well as information on their experiences with infertility and loss in the past. One should have a complete physical and a gynecological checkup. investigation of tubal patency through hysterosalpingogram or laparoscopy; vaginal ultrasound; hormonal test in CD3; infertility workup. The spouse was also given a complete medical history and his seminal fluid was analyzed; the results of the seminal fluid examination were evaluated by WHO 2010 standards. The aromatase inhibitor pill (Gynotril 2.5 mg), which was administered orally twice daily at intervals of 12 hours starting on day 3 and continuing for a total of five days, was given to the women who participated in the trial. At CD3, a hormonal test (including FSH, LH, Progesterone, prolactin, E2, and AMH), as well as an evaluation of antral follicle counts and endometrial thickness using ultrasound, were performed. Starting on day 9, a serial ultrasound was performed every other day until at least one developed follicle measuring less than 17 millimeters in diameter was found. On the day before the trigger, every patient has another round of hormonal testing, including LH, FSH, E2, and progesterone. Another evaluation for sub-endometrial blood flow, endometrial pattern, and endometrial thickness Patients are divided into three categories according to the kind of triggers they experience:

1 .Group A: women in the research group were given injections of both a dual trigger and an (Ovitrelle 250 mg plus FSH 150 IU Gonal f).

2 .Group B: On the day of the trigger, women in the trial group were given an injection containing both Ovitrelle (250 mg) and follitropin-stimulating hormone (75 IU).

3 .Group C: Only female participants were given Ovitrelle (250 mg).

To confirm ovulation on the day of the IUI, vaginal ultrasound was carried out between 36 and 48 hours after the ovulation trigger was administered This was done by measuring the endometrium and analyzing its significance as well as by determining how much blood is flowing outside of the uterine lining. A blood sample was taken that day to do a hormonal assay to identify FSH, LH, progesterone, and E2. The normal hormonal levels that were employed in the investigation are listed in **Table 1**. On the day of the IUI, the patient started using a progesterone vaginal suppository with 400 mg daily to aid in the luteal phase. This treatment lasted for two weeks. (In the United Kingdom, Cyclogest® 400mg is sold under the name "Cyclogest"). Beta human chorionic gonadotropin estimation 14 days after in vitro fertilization.

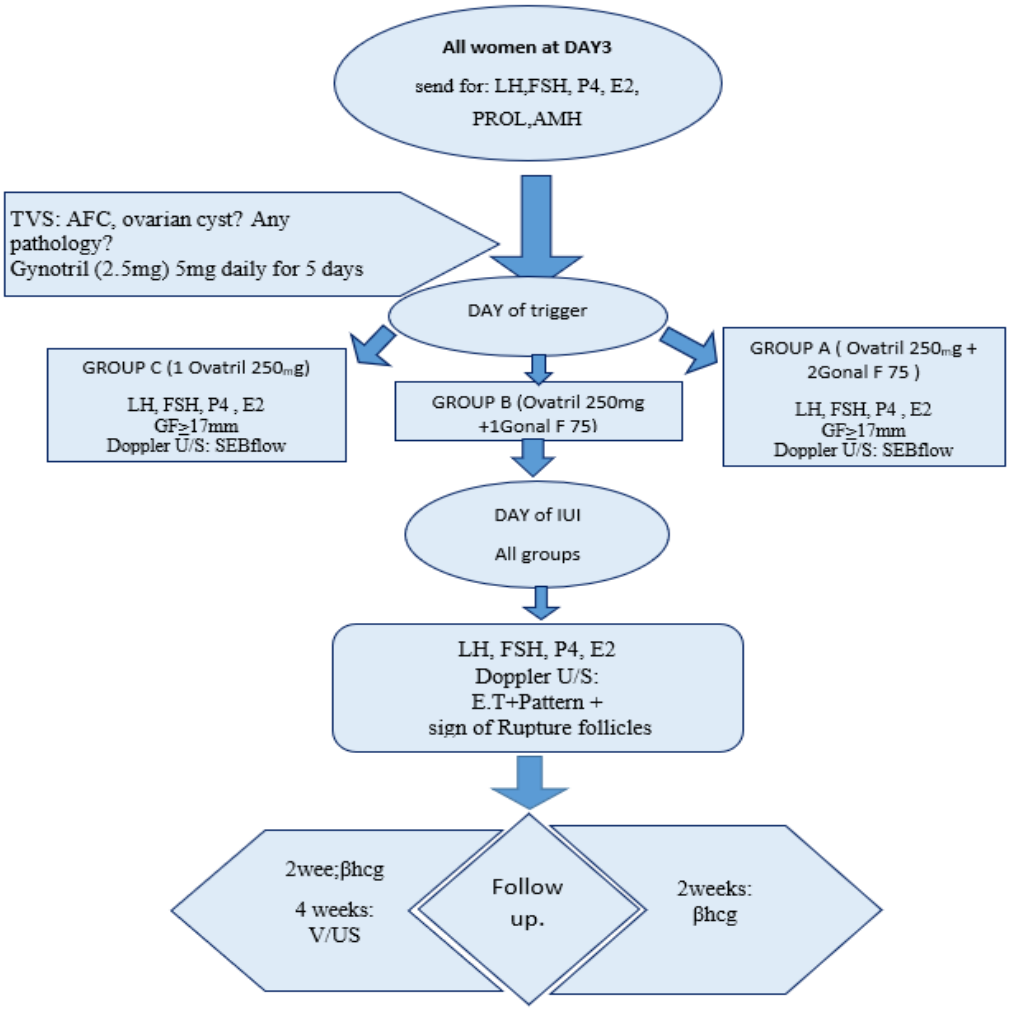


**Figure 1: Study design**

Before being accepted into the study, every pair was given an infertility test that included a careful history and physical examination, as well as the age of the female and the male spouse. The length of infertility and its underlying reason, menstruation history, prior pregnancies and losses, history of illnesses, use of cigarettes, medicines, or surgery, and any previous infertility diagnoses or treatments, such as IUI or IVF. Knowing the person's sexual history, including how often they have sexual encounters and if they have ever used birth control, is also crucial. Then, we obtained the patients' duly written informed permission.

On cycle day 3, a blood sample was taken from each woman as part of the workup to get a baseline measurement of the hormones FSH, LH, E2, progesterone, AMH, and prolactin. As part of the workup, this was completed. Additionally, a thyroid function test, often referred to as TSH, will be carried out as a screening for thyroid function. Serum LH, FSH, E2, and progesterone levels were assessed on the day when ovulation was triggered (days 11–14). When the ovulation was verified, a second blood sample was taken on the day of the IUI (36–48 hours after the triggering) and utilized for hormonal analysis (FSH, LH, Progesterone, E2).

The transvaginal scan was completed by using the ultrasound device's vaginal probe (vinno35, china). After placing patients in the dorsal lithotomy posture with an empty bladder, an early follicular ultrasound (CD 2-3) was carried out to count the number of antral follicles, gauge the thickness of the endometrium, and rule out the presence of ovarian cysts or other pathologies. The ultrasound was then performed once again in the middle of the cycle (CD9–14) to see whether a mature follicle had been discovered. A sweep of the mid-sagittal plane of the uterus was performed after employing an ultrasound device to provide a multiplane display. The greatest distance from one basal endometrial interface through the endometrial canal to the opposing endometrial-myometrial interface of the anterior to the posterior wall of the uterus was used to determine the endometrial thickness, which was measured in the median longitudinal plane of the uterus. This measurement was made between the uterus' anterior and posterior walls). There must be at least one dominant follicle that is greater than 17 millimeters in diameter for an IUI procedure to be successful. Additionally, as shown in **Figure 1**, a triple-line pattern and an ET of less than 8 millimeters are strongly associated with successful implantation. (3.4). Depending on how it appeared, the pattern of the endometrium was classified as multilayered or non-multilayered. A Type A triple-line pattern, with hyperechogenic outer lines, a distinct core echogenic line, and hypoechogenic or dark patches in between these lines, represented a multilayered endometrium. It was observed that the center echogenic line was well delineated. neutral in attitude (same reflectivity of the endometrium as

the surrounding myometrium and poorly defined central echogenic line-Type B), A homogeneous endometrial pattern that is either hyperechogenic or echogenic makes up one kind of endometrium, called a non-multilayered endometrium.

For endometrial assessment, a sonographic examination of endometrial thickness and texture has been employed. Every ultrasound exam I've seen has included switching to color Doppler once a longitudinal picture of the uterus has been taken. Our ability to identify the sub-endometrial blood flow distribution pattern was made possible using pulsating color signals shown in the sub-endometrial and endometrial regions. those patients who have vascularization that has penetrated the sub endometrium. Zone 1 included vessels that entered the outer hypoechogenic area surrounding the endometrium but did not penetrate the hyperechogenic outer margin; Zone 2 included vessels that entered the hyperechogenic outer margin but did not penetrate the hypoechogenic inner area; Zone 3 included vessels that entered the hypoechogenic inner area; and Zone 4 included vessels that reached the central echogenicity of the endometrium.

After that, Doppler sonography was done on the blood vessels that had the most prominent coloration within the innermost part of the endometrial and sub-sub-endometrial. After ensuring that there were no gaps in the waveforms, a cardiac cycle average of three to five beats was selected to calculate the resistance index (RI) and the pulsatility index (PI). We took three separate readings for each parameter, and then we calculated the average of those readings. The resistance index (RI) and pulsatility index (PI) of the sub-endometrial arteries were automatically calculated by ultrasonography. The sub-endometrial zone was regarded to be within 1 mm of the myometrial–endometrial contour when it was first described. When a patient's medical history or physical examination revealed evidence of previous damage to the Fallopian tube as a result of pelvic inflammatory disease (PID) or previous surgery, endometriosis, hysterosalpingography, and/or laparoscopy were performed to evaluate the tube's patency, and determine whether or not it was intact. In addition, congenital deformities of the uterus, such as a bicornuate uterus, were not taken into consideration.

## 3. Results

All hormonal markers (**Table 1**) showed no statistically significant differences ($P>0.05$) between research groups.

**Table 1: Indicator-day clinical parameter comparisons between study groups**

| Clinical parameter On the day of the trigger | Study group | | | P - Value |
|---|---|---|---|---|
| | A Mean ± SD | B Mean ± SD | C Mean ± SD | |
| **LH (IU/L)** | 15.49 ± 10.6 | 14.11 ± 8.5 | 17.96 ± 14.5 | **0.386** |
| **FSH (IU/L)** | 5.92 ± 2.6 | 6.05 ± 3.3 | 6.2 ± 4.7 | **0.954** |
| **Progesterone (ng/mL)** | 0.38 ± 0.38 | 0.35 ± 0.36 | 0.55 ± 0.38 | **0.073** |
| **E2 (pg/mL)** | 195.33 ± 98.7 | 183.78 ± 99.5 | 160.54 ± 79.8 | **0.271** |

The table below compares the hormonal parameters of the study groups on the day of IUI (2). With a median of 6.98 IU/L, group C's FSH was significantly lower than groups A and B's (9.06 and 9.3 IU/L, respectively; P=0.031). A statistically significant difference was found between Group A's average E2 concentration of 69.62 pg/mL and Groups B and C's concentrations of 53.32 and 36.65 pg/mL. (P 0.001). No significant changes between groups were seen for any of the other hormonal variables (P> 0.05).

**Table 2: Clinical parameters on the day of IUI compared across research groups.**

| Clinical parameter On the day of IUI | Study group | | | P - Value |
|---|---|---|---|---|
| | A Mean ± SD | B Mean ± SD | C Mean ± SD | |
| **LH (IU/L)** | 19.96 ± 11.1 | 24.65 ± 11.5 | 22.01 ± 12.4 | **0.24** |
| **FSH (IU/L)** | 9.06 ± 3.7 | 9.3 ± 4.3 | 6.98 ± 3.02 | **0.031** |
| **Progesterone (ng/mL)** | 1.78 ± 1.4 | 1.87 ± 1.7 | 2.14 ± 1.6 | **0.655** |
| **E2 (pg/mL)** | 69.62 ± 45.0 | 53.32 ± 33.1 | 36.65 ± 24.0 | **0.001** |

When comparing E2 levels on the day of the trigger to the day of the IUI, we found that in group C, the difference was statistically significant (P=0.036). All other hormonal markers showed no statistically significant variation between research groups on the day of IUI compared to the day of trigger (P> 0.05).

**Table 3: Clinical parameter comparison between IUI and trigger day in terms of % change**

| What difference between IUI day and trigger day as a percentage | Study group | | | P - Value |
|---|---|---|---|---|
| | A Mean ± SD | B Mean ± SD | C Mean ± SD | |
| **LH** | 72.45 ± 104.8 | 124.75 ± 138.6 | 89.88 ± 138.8 | **0.22** |
| **FSH** | 70.29 ± 74.2 | 80.57 ± 83.9 | 47.68 ± 79.9 | **0.247** |
| **Progesterone** | 734.66 ± 865.7 | 629.07 ± 609.9 | 455.08 ± 506.6 | **0.271** |
| **E2** | - 61.23 ± 24.2 | - 67.17 ± 19.2 | - 74.13 ± 18.2 | **0.036** |

The comparison in baseline clinical parameters between study groups is shown in **Table 4**. No statistically significant differences (P≥ 0.05) between study groups regarding all baseline clinical parameters.

**Table 4: Comparison in baseline clinical parameters (at cycle day 2) between study groups**

| Baseline clinical parameter | Study group | | | P - Value |
|---|---|---|---|---|
| | A Mean ± SD | B Mean ± SD | C Mean ± SD | |
| **AFC (Count)** | 12.31 ± 3.9 | 13.81 ± 3.8 | 12.1 ± 2.9 | **0.099** |
| **Endometrial thickness (mm)** | 4.73 ± 0.9 | 4.56 ± 1.0 | 4.78 ± 1.2 | **0.665** |

The comparison in clinical parameters between study groups on the day of the trigger is shown in **Table 8**. No significant differences between study groups (P ≥ 0.05) in all clinical parameters.

**Table 5: Comparison between study groups in clinical parameters on the day of the trigger**

| Clinical parameter on the day of the trigger | Study group | | | P - Value |
|---|---|---|---|---|
| | A Mean ± SD | B Mean ± SD | C Mean ± SD | |
| **Endometrial thickness (mm)** | 8.06 ± 1.5 | 8.15 ± 1.5 | 8.23 ± 2.0 | **0.919** |
| **Resistance Index** | 0.62 ± 0.07 | 0.59 ± 0.04 | 0.59 ± 0.06 | **0.092** |
| **Pulsatile Index** | 1.07 ± 0.2 | 1.04 ± 0.2 | 1.01 ± 0.2 | **0.553** |
| **S/D** | 2.65 ± 0.5 | 2.52 ± 0.3 | 2.53 ± 0.3 | **0.311** |
| **Follicle number** | 1.28 ± 0.5 | 1.51 ± 0.5 | 1.34 ± 0.5 | **0.145** |
| **Endometrial pattern No. (%) No. (%) No. (%)** | | | | |
| **hypoechoic endometrium A** | 25 (71.4) | 24 (64.9) | 20 (69.0) | **0.694** |
| **Isoechoic endometrium B** | 10 (28.6) | 13 (35.1) | 9 (31.0) | |

Clinical parameters comparing research groups on the day of IUI are shown in **Table 6**. All other clinical measures showed no significant group differences (P > 0.05).

**Table 6: Clinical parameters on the day of IUI compared across study groups.**

| Clinical parameters on the day of IUI | Study group | | | P - Value |
|---|---|---|---|---|
| | A Mean ± SD | B Mean ± SD | C Mean ± SD | |
| **Endometrial thickness (mm)** | 9.76 ± 1.5 | 9.32 ± 1.6 | 8.9 ± 1.8 | **0.115** |
| **Resistance Index** | 0.58 ± 0.07 | 0.61 ± 0.06 | 0.57 ± 0.06 | **0.074** |
| **Pulsatile Index** | 1.0 ± 0.19 | 1.03 ± 0.18 | 0.95 ± 0.2 | **0.286** |
| **S/D** | 2.51 ± 0.5 | 2.6 ± 0.4 | 2.35 ± 0.4 | **0.067** |
| **Endometrial pattern No. (%) No. (%) No. (%)** | | | | |
| **B** | 33 (94.3) | 34 (91.9) | 27 (93.2) | **0.542** |
| **A** | 2 (5.7) | 3 (8.1) | 2(6.8) | |

**Table 7** shows the percentage change between the day of IUI and the day of the trigger for each research group. Also, in comparison to the day of the trigger, RI was lower in group A on the day of IUI (P= 0.003) than in either of the other two groups (B and C). All other clinical parameters showed no statistically significant difference between research groups on the day of IUI compared to the day of trigger (P> 0.05).

**Table 7: A cross-sectional research comparing several clinical parameters on the day of IUI and the day of trigger across the study groups.**

| Difference between IUI day and trigger day as a percentage | Study group | | | P - Value |
|---|---|---|---|---|
| | A<br>Mean ± SD | B<br>Mean ± SD | C<br>Mean ± SD | |
| **Endometrial thickness** | 22.98 ± 18.6 | 15.94 ± 17.5 | 9.43 ± 11.3 | **0.006** |
| **Resistance Index** | - 6.21 ± 9.4 | - 3.14 ± 13.3 | 3.13 ± 11.5 | **0.003** |
| **Pulsatile Index** | - 4.91 ± 14.3 | 1.77 ± 21.0 | - 3.36 ± 24.1 | **0.337** |
| **S/D** | - 3.17 ± 21.1 | 4.08 ± 18.6 | - 6.27 ± 16.0 | **0.073** |

## 4. Discussion

Baseline hormonal parameters for each study group are shown in **Table 1** below. All the studied groups showed similar levels of FSH, LH, progesterone, and estradiol at baseline, with no statistically significant differences (P values 0.05) between the groups. Similar research conducted by **[6]** Younis et al. and Mahajan et al. **[7]** found no statistically significant differences in demographics (age, BMI, baseline FSH, LH, and AMH levels) or infertility risk factors (causes). Baseline variables including age, BMI, basal FSH, and LH did not vary substantially across groups, demonstrating this. Declare et al. **[8]** found no statistically significant difference in the time course of hormone changes between the two groups when comparing estradiol and progesterone levels on a triggering day. Both hormones shared this property. This can be explained by the fact that all the participants in the research took the same drug during the induction phase. Our findings agreed with those found in a different study carried out by Lamb, **[2]**. Women who underwent a prolonged GnRHa regimen were included in this trial, and an FSH supplement was administered around the time of the hCG trigger. Increased blood FSH levels were reported in both investigations, however, one research did so before oocyte extraction and the other after. Researchers in this research took into account the fact that women often have greater FSH levels in their blood on the day of oocyte extraction than they do on the day before the procedure. Another study found that a decrease in E levels after hCG administration did not alter pregnancy outcomes. The number of eggs that were

recovered, the number of mature oocytes, and the fertilization rates were all unaffected by the decrease in E. [9]. According to the findings of Chiasson [10], a drop in E2 levels following the injection of hCG for 24 hours did not affect the results of the pregnancy. The number of eggs that were recovered, the number of mature oocytes, and the fertilization rates were all unaffected by the decrease in E2. As no significant difference in implantation rates was revealed with either an increase or decrease in E levels following hCG injection, it seems that estradiol levels do not play a role in priming the endometrium for implantation. In addition, there was no correlation between endometrial receptivity priming and estrogen concentrations.

According to the findings of morad [11], letrozole is an effective second-line therapy for women with poor endometrial response to CC. This is because letrozole enhanced endometrial thickness in a trilaminar pattern and improved endometrial perfusion. When comparing the endometrial thickness of group A to that of groups B and C on the day of IUI, group A demonstrated a considerably greater rise (P = 0.006) and a significantly greater drop (P = 0.003) in endometrial thickness than group B and C did. This may be understood by considering the simultaneous rise in the E2 level that was discovered previously in this study. It was discovered by Ciechanowska et al. [12] that many different variables had been evaluated as potential predictors of endometrial thickness. In women, these variables include age, BMI, total exogenous FSH/highly purified human menopausal gonadotrophin dosage, ovarian stimulation time, and oestradiol and progesterone levels during the late follicular phase. This explains why our research indicated that there was an increase in endometrial thickness when the fish bolus dose was detected at the time of the trigger.

When comparing the RI in Group A on the day of IUI to the RI in Groups B and C on the day of the trigger, the researchers observed that Group A had a statistically significant drop in sub-endometrial blood flow (P = 0.003). To explain this finding, Ng et al. demonstrated that increased blood E2 concentration during ovarian stimulation causes vasodilation, particularly in the myometrium (2007). Blood flow in the uterus, endometrium and sub-endometrium are all linked during normal, stimulated menstrual cycles. The endometrium and sub-endometrium get less blood supply during ovarian stimulation. It was discovered that monitoring uterine blood flow is not an accurate surrogate for endometrial blood flow[13], even during stimulated cycles found that rFSH and uFSH were able to differently influence the gene expressions in human endometrial stromal cells that were cultivated in vitro[14]. According to the findings of their research, fsh has several beneficial effects on the expression of genes involved in implantation, including an increase in endometrial receptivity. Aromatase transcription was

also found in the endometrium of individuals who were unable to conceive, even though the levels were quite variable between samples. As a result, FSH may affect endometrial aromatase, leading to an increase in local estrogen production. After using the FSH/LH trigger, endometrial receptivity indicators were found to have greatly increased, despite an increase in endometrial thickness and a large reduction in resistance index. Since it considerably increases endometrial thickness, the dual trigger FSH / LH might be a viable alternative therapy for individuals who have a thin endometrium. Both the examination of sub-endometrial blood flow by 2D ultrasonography and the determination of follicle development are important aspects of the procedure. More studies are required to compare the success rate of pregnancy in women with normal endometrial thickness to those in women with thin endometrium when using the dual triggerfish/lh.

## 5. Reference


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