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THE PREDICTIVE VALUE OF ENDOMETRIAL THICKNESS AND PATTERN ON REPRODUCTIVE OUTCOME IN THE FIRST FRESH IVF/ICSI CYCLE

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Abstract

The endometrium plays a crucial role in successful implantation during assisted reproductive techniques such as in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI). Prior research has established a correlation between endometrial thickness and reproductive outcomes; however, the optimal thickness for improved live birth rates (LBR) remains debated. This study aimed to investigate the relationship between endometrial thickness and the live birth rate in IVF/ICSI cycles, while also assessing the impact of endometrial pattern independent of thickness. A retrospective analysis was conducted on patients undergoing IVF/ICSI treatments between [insert study period]. Endometrial thickness was measured via transvaginal ultrasound prior to embryo transfer. Participants were divided into groups based on thickness: <8 mm, 8-11 mm, 12-14 mm, and >14 mm. Clinical pregnancy rates and LBRs were compared across these groups. The findings revealed that endometrial thickness of 8 mm or greater significantly correlated with improved LBR. Notably, participants with thickness above 11 mm exhibited the highest clinical pregnancy rates, with a plateau observed at 14 mm, after which a decrease in outcomes was noted. Furthermore, the endometrial pattern demonstrated a significant association with reproductive success independent of thickness, suggesting it is an essential factor in the IVF process. This study confirms that adequate endometrial thickness is vital for favorable IVF/ICSI outcomes, with optimal thickness observed at 11 mm. Moreover, the endometrial pattern significantly influences reproductive success, indicating that both thickness and morphological characteristics should be considered in clinical practice. Future studies with larger sample sizes are required to further elucidate the predictive effects of endometrial parameters on IVF/ICSI success.

Keywords:

Endometrial Thickness - IVF (In Vitro Fertilization) - ICSI (Intracytoplasmic Sperm Injection) - Endometrial Pattern - Assisted Reproductive Technology (ART) -Endometrial Receptivity - Embryo Implantation

1- INTRODUCTION

1-1- Research Background

In vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) have become critical advancements in reproductive medicine, offering hope to couples facing infertility. One of the key factors influencing the success of these procedures is the endometrium, the innermost lining of the uterus, which plays a vital role in implantation and subsequent pregnancy viability. The endometrial thickness (EMT) and pattern are considered significant indicators of endometrial receptivity and, consequently, the likelihood of achieving a successful pregnancy. Identifying reliable predictors of reproductive outcomes is essential for optimizing IVF/ICSI protocols and improving clinical practices. The endometrium undergoes cyclical changes governed by hormonal fluctuations, and its optimal thickness is critical for embryo implantation. Studies have shown that an EMT of 7 to 14 mm is generally associated with favorable reproductive outcomes, whereas significantly thinner or thicker endometria may correlate with reduced implantation rates and increased miscarriage risks. However, the ideal values can vary depending on the population studied and the specific protocols employed in IVF/ICSI treatments. Furthermore, the echogenicity and pattern of the endometrial lining observed through transvaginal ultrasound may provide additional information concerning its receptivity, influencing implantation success.

Emerging research emphasizes the importance of taking a multi-faceted approach to assess endometrial characteristics. Endometrial morphology is not only defined by thickness; changes in pattern and texture can also be informative. The trilaminar echogenic pattern, for example, has been associated with increased implantation rates compared to a homogeneous or non-trilaminar pattern. Despite these findings, there remains a lack of consensus among the studies regarding the exact predictive thresholds for EMT and endometrial pattern, potentially due to differences in methodologies, population demographics, and the retrospective nature of most studies.

The focus of this study is on a specific population: couples undergoing their first fresh IVF/ICSI cycle. The decision to include only the first cycle is pivotal, as repeated cycles may introduce confounding variables that can distort the connection between endometrial characteristics and reproductive outcomes. By narrowing the scope to first fresh cycles, the study aims to reduce the variability introduced by repeated attempts and thus enhance the reliability of the findings.

The clinical implications of determining the predictive value of EMT and pattern on reproductive outcomes are significant. Improvement in the selection criteria and personalized treatment plans for patients can lead to higher success rates in IVF procedures. Furthermore, earlier identification of patients at risk of poor outcomes can enable timely interventions or consideration of alternative reproductive options, such as donor sperm or eggs or even surrogacy.

1-2- Research Problem

Despite the increasingly widespread use of IVF and ICSI as solutions for infertility, the variability in success rates remains a significant challenge in assisted reproductive technology. Endometrial receptivity is a critical factor determining the success of embryo implantation, yet there is considerable uncertainty surrounding the optimal endometrial thickness and pattern that predicts favorable reproductive outcomes in fresh embryo transfers. Existing literature often presents conflicting evidence regarding the thresholds of EMT that correlate with successful pregnancies. Consequently, many practitioners grapple with establishing standardized protocols that can uniformly predict successful implantation and ongoing pregnancies.

Several studies have noted correlation between endometrial thickness and reproductive outcomes, concluding that certain thickness measurements are associated with improved rates of implantation and clinical pregnancy. However, there is a lack of consensus on precise EMT values, as some studies pinpoint a thickness of 8-10 mm as optimal, while others report success using a broader range. This inconsistency is compounded by the inclusion of diverse populations, embryos, and treatment protocols, making it difficult for clinicians to rely on established guidelines.

The role of the endometrial pattern adds another layer of complexity to the evaluation of endometrial receptivity. While a trilaminar pattern is typically deemed favorable, interpretations of non-trilaminar patterns vary significantly across studies. Clinicians often find themselves at a crossroad without clearly defined metrics for determining which endometrial characteristics predict the best outcomes for their patients. This ambiguity can lead to suboptimal embryo transfer decisions, ultimately affecting patients' chances of achieving pregnancy during IVF/ICSI cycles.

Additionally, the retrospective nature of many studies limits the ability to definitively establish cause-and-effect relationships between endometrial characteristics and reproductive outcomes. Historical data may be subject to various biases, missing information, and inconsistencies in data collection, further clouding the interpretation of findings. The complex interplay between factors such as age, body mass index, hormone levels, and previous fertility history also complicates the relationship between EMT/pattern and outcomes.

In light of these challenges, this study proposes to investigate the predictive value of endometrial thickness and pattern in relation to reproductive outcomes specifically within the context of the first fresh IVF/ICSI cycle. By concentrating on a homogenous population and eliminating potential confounding factors stemming from multiple cycles, this research aims to provide clearer insights into the specific characteristics of the endometrium that can reliably predict successful embryo implantation and subsequent pregnancy. This clearer understanding may, in turn, inform clinical decision-making for practitioners, contributing to enhanced reproductive success rates.

1-3- Aims & Objectives

The main aim of this study is to evaluate the predictive value of EMT in reproductive outcome of fresh embryo transfers in IVF/ICSI cycles. Only first t fresh IVF/ICSI cycle for each couple were included given the effect of multiple repeated cycle on the accuracy and reliability of the outcomes.

Objectives:

1. To assess the correlation between endometrial thickness measurements and the rates of clinical pregnancy in first fresh IVF/ICSI cycles.
2. To analyze endometrial patterns (trilaminar vs. non-trilaminar) and their association with implantation success and pregnancy outcomes.
3. To identify optimal thresholds of endometrial thickness that predict successful reproductive outcomes based on a retrospective review of clinical data.
4. To evaluate the impact of patient demographics and clinical characteristics on the relationship between EMT/pattern and reproductive success.

1-4- Research Significance

The significance of this study lies in its potential to improve clinical practices in reproductive medicine by providing clear, evidence-based insights into the role of endometrial thickness and pattern in predicting reproductive outcomes for fresh IVF/ICSI cycles. As infertility rates continue to rise globally, optimizing the effectiveness of assisted reproductive technologies has never been more critical. By examining the predictive value of endometrial characteristics, this research aims to contribute to a more nuanced understanding of endometrial receptivity, which can directly influence both clinical decision-making and patient counseling.

The study offers the promise of refining embryo transfer protocols. By determining specific EMT and pattern thresholds associated with successful outcomes, clinicians can make informed decisions regarding the timing and approach to embryo transfer. This could potentially lead to enhanced success rates, streamlined patient care, and reduced emotional and financial burdens on couples undergoing fertility treatments.

This research can enhance our understanding of individual variability in reproductive outcomes. By focusing on a population of couples experiencing their first fresh IVF/ICSI cycle, the study aims to mitigate confounding variables that often cloud results in larger, more heterogeneous studies. This enhanced clarity could reveal more tailored treatment strategies and preparedness, allowing for targeted interventions for patients whose endometrial characteristics deviate from established norms.

The findings may serve as a foundation for future research endeavors. Establishing robust correlations between endometrial features and reproductive success can instigate further studies that explore the underlying biological mechanisms influencing these relationships. Such insights could advance the field of reproductive medicine, potentially leading to novel methodologies that optimize endometrial conditions for embryo implantation.

As healthcare systems and professionals increasingly prioritize evidence-based practices, the outcomes of this study can align with contemporary movements advocating for personalized medicine in reproductive health. Providing clinicians with specific benchmarks for evaluating endometrial receptivity aligns well with broader trends toward individualized treatment plans, ensuring that patients receive the most tailored and effective care possible. This research holds the potential to impact clinical practice, enhance patient outcomes, and lay the groundwork for future exploration into the complex interplay between endometrial factors and reproductive success in assisted reproductive technology.

2- LITERATURE REVIEW

In recent decades, extensive research has focused on the multifactorial nature of implantation and live birth success rates in assisted reproductive technology (ART), particularly in IVF and ICSI procedures. Various maternal and embryonic factors have been identified, with notable emphasis on maternal age, body mass index (BMI), and, crucially, endometrial receptivity indicators, notably endometrial thickness (EMT). Understanding the role of these factors is imperative for optimizing ART outcomes.

Advanced maternal age is one of the most documented factors that negatively impact IVF outcomes. Research consistently shows that fertility decreases significantly with age, primarily due to a decline in oocyte quantity and quality. The maternal included age and body mass index, many studies showed a negative impact on IVF outcomes is associated with advanced maternal age and elevated BMI more than 30 (Lv, et al., 2020). A comprehensive study by Cobo et al. (2016) demonstrated that women beyond 35 years exhibit reduced implantation and clinical pregnancy rates, leading to higher miscarriage rates. The accumulated age-related genetic anomalies in oocytes can also affect the developmental competence of embryos, thereby impacting pregnancy outcomes (Liu et al., 2017).

Elevated BMI is another crucial maternal factor linked to adverse IVF outcomes. Excessive weight, defined as a BMI over 30, has been associated with decreased ovarian response, altered hormone levels, and detrimental endometrial environment. A systematic review by Rubino et al. (2016) emphasized that high BMI not only affects oocyte quality but also likely contributes to impaired endometrial receptivity. Conversely, underweight individuals also face challenges, albeit through different biological mechanisms affecting hormonal balance and ovarian reserve (Tirado-González et al., 2017).

Endometrial receptivity was also studied, as unique dynamic changes occur in this hormonally responsive tissue. Hormonal effect induces dramatic molecular, histopathological, and immunological changes throughout menstrual cycle. The aim of those changes is preparation for the potential implantation of hatched embryo (Gellersen and Brosens, 2014). The endometrium's role in the success of implantation has gained considerable attention, as it undergoes dynamic changes throughout the menstrual cycle, influenced by hormonal variations. Key processes such as decidualization, angiogenesis, and the expression of specific adhesive proteins are central to establishing a receptive endometrial environment for embryo implantation.

Endometrium undergoes decidualization, the differentiation of stromal fibroblasts to "epithelioid" cells, after mid cycle LH (luteinizing hormone) surge and endometrium progesterone exposure. This key preparatory step is mandatory for the establishment and maintenance of pregnancy. Decidualization is the transformation of the endometrial stromal cells to a specialized phenotype following the mid-cycle LH surge and subsequent progesterone exposure. This process is essential for creating a conducive microenvironment for implantation. The changes accompany an increase in vascular permeability and immunological adaptations that facilitate successful implantation (González et al., 2012). The disruption of any of these processes can lead to implantation failure, emphasizing the importance of evaluating endometrial changes in ART cycles.

EMT is one of the primary indicators of endometrial receptivity. Studies have shown that there is an optimal range of EMT, generally between 7 to 14 mm, associated with better implantation and live birth rates (Sharma et al., 2018). However, the optimal EMT can vary depending on multiple factors, including the individual's age and hormonal environment. A prospective cohort study by Mazurkiewicz et al. (2021) found that women with EMT less than 7 mm exhibited significantly lower implantation rates, reinforcing the importance of monitoring EMT during ART cycles.

In stimulated cycles endometrial thickness on the day of human chorionic gonadotropin (HCG) administration is used as indicator of endometrial receptivity (Gellersen and Brosens, 2014). Other markers for receptivity include endometrial pattern, endometrial volume, and endometrial and sub-endometrial blood flow. Iimmunological and molecular marker also play role in evaluation of receptivity (Lv, et al., 2020). Although numerous studies have already been conducted and focused on the relationship between EMT and IVF outcomes, there is no consensus reached and remained controversial (Kasius et al., 2014; Schild et al., 2001). The potential reasons for this discordant result could be due to multiple confounders which include maternal age, quality of embryos, and variability in ovarian stimulation protocols. Despite this, EMT assessment still used by clinician during IVF stimulation cycle as it is easy and non-invasive tool (Gao et al., 2020; Alcázar, 2006).

Beyond thickness, the echogenic pattern of the endometrium assessed through transvaginal ultrasound presents additional insights into endometrial receptivity. A trilaminar pattern is often considered a positive indicator for implantation potential compared to a non-trilaminar configuration. Studies such as those by Suryavanshi et al. (2018) have established strong correlations between a trilaminar endometrial pattern and higher clinical pregnancy rates. These patterns reflect the hormonal influence on the endometrium during the luteal phase, with changes in echogenicity indicative of receptivity.

Endometrial and sub-endometrial blood flow, assessed through Doppler ultrasonography, provides further information about endometrial viability and receptivity. Proper angiogenesis is vital for supplying nutrients and oxygen to the developing embryo. A meta-analysis by Zhang et al. (2020) showed that effective endometrial perfusion is positively correlated with IVF success rates. Increased blood flow to the endometrium correlates with the reinforcement of decidualization and a more favorable implantation site.

In addition to structural assessment, molecular markers have emerged as valuable indicators of endometrial receptivity. Cytokines, integrins, and hormone receptors play crucial roles in the implantation process (Zhou et al., 2018). For instance, elevated levels of interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) have been associated with adverse outcomes during the implantation window, suggesting a complex interplay between the immune response and implantation success.

3- Materials and methods

3-1- Study design

This study employed a retrospective cohort design to evaluate the impact of endometrial thickness and pattern on the reproductive outcomes of fresh IVF/ICSI cycles. Clinical data were meticulously reviewed from the reproductive unit of the Prince Sultan Military Medical City in Riyadh, spanning from October 2017 to September 2020. The study protocol received ethics approval from the Ethics Committee of Prince Sultan Military Medical City, ensuring compliance with ethical standards in human research.

Inclusion Criteria:

The study included fresh IVF/ICSI cycles that met the following criteria:

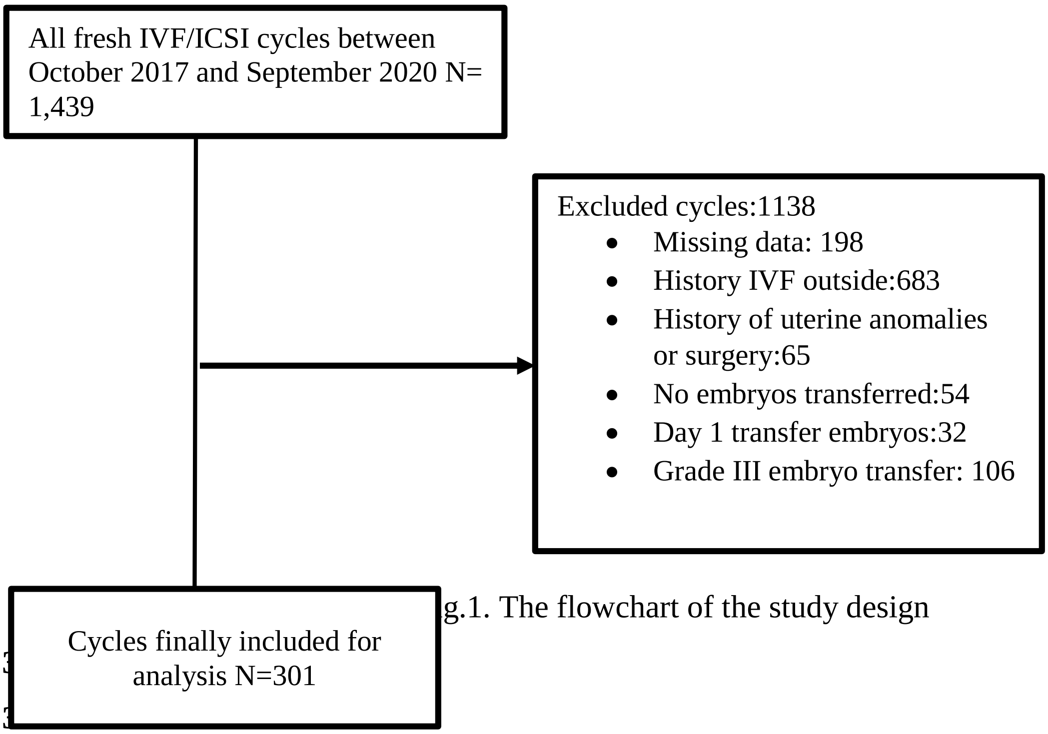
- First IVF/ICSI cycle for each couple to eliminate biases associated with previous cycles.
- Cycles stimulated using either Gonadotropin-Releasing Hormone (GnRH) agonist or antagonist protocols.
- Administration of human chorionic gonadotropin (HCG) to trigger final oocyte maturation at doses of 5000 IU, 10000 IU, or recombinant HCG.
- Transvaginal ultrasound evaluation of endometrial thickness on the day of HCG administration.

Exclusion Criteria:

The following factors were used to exclude cycles from the study:

- A history of uterine surgery or anatomical anomalies.
- Transfer of 2 pronucleus stage embryos or embryos graded as Grade III according to established embryo classification systems.

A total of 301 cycles qualified and were included in the final analysis. A flowchart depicting the study design and enrollment process is provided in Figure 1.



g.1. The flowchart of the study design

Baseline characteristics of the study participants were collected from medical records in the reproductive unit, encompassing both demographic and fertility-related variables.

Demographic Information:

- Maternal Age: Age of the female partner at the time of treatment initiation, categorized into age groups for analysis (e.g., <30, 30-34, 35-39, ≥40).
- Parity: The number of previous pregnancies carried to a gestational age of 20 weeks or more.
- Body Mass Index (BMI): Calculated as weight in kilograms divided by the square of height in meters. BMI was categorized according to the World Health Organization classifications (underweight: <18.5, normal: 18.5-24.9, overweight: 25-29.9, obese: ≥30).

Fertility Characteristics:

- Basal Serum Levels: Baseline serum levels of Follicular Stimulating Hormone (FSH) and Estradiol (E2) were measured on day 2 or 3 of the menstrual cycle.
- Cause of Infertility: The primary etiology of infertility was categorized into:
    a. Male factor
    b. Anovulation
    c. Tubal factor
    d. Poor ovarian reserve
    e. Unexplained infertility
    f. Multiple factors.

3-4- Treatment characteristics

Various treatment parameters gathered during the IVF/ICSI cycles included:

- Gonadotropin Dosage and Duration: Total dosage and duration of recombinant FSH (rFSH) or other gonadotropins, tracked during each cycle to assess stimulation response.
- Cycle Protocols: Documented protocols utilized (long agonist or antagonist) to elucidate any impacts on endometrial receptivity.
- Serum Levels on HCG Day: Recorded serum estradiol and progesterone levels on the day of HCG administration to monitor hormonal status.
- Embryo Transfer Details: Included:
  a. Stage of Embryos: Cleavage stage (Day 3) or blastocyst stage (Day 5).
  b. Number of Embryos Transferred: Indicated the total number of transferred embryos during the procedure.
- Oocyte Retrieval: The total number of oocytes retrieved was noted, tracking the ovarian response to stimulation protocols.

3-5- Assisted reproductive technique protocol

Long pituitary down regulation protocol

All patient who planned for long protocol were given 0.1 mg Gnrh agonist (triptorelin; Decapeptyl, Ferring, West Drayton, UK), started at the mid luteal phase and continued till HCG trigger day. Down regulated patients were started on daily calculated dose of recombinant FSH (rFSH: Gonal-F®, Merck Pharmaceuticals, Darmstad, Germany); human menopausal gonadotrophin (Menogon®, Ferring Pharmaceuticals, St. Prex, Switzerland) or highly purified human menopausal gonadotrophin (HP-HMG; Menopur®, Ferring Pharmaceuticals, St. Prex, Switzerland). Dose range between (150-450IU).

Gonadotropin releasing hormone antagonist protocol

Patients who were assigned for this protocol received individually calculated daily dose of recombinant FSH (rFSH: Gonal-F®, Merck Pharmaceuticals, Darmstad, Germany); human menopausal gonadotrophin (Menogon®, Ferring Pharmaceuticals, St. Prex, Switzerland) or highly purified human menopausal gonadotrophin (HP-HMG; Menopur®, Ferring Pharmaceuticals, St. Prex, Switzerland). Dose range between (150-450IU). GnRH antagonist cetrorelix (Cetrotide®, Merck Pharmaceuticals) daily dose started from day 6 of stimulation and continued till HCG Day.

Patients follow up and ultrasound assessment of endometrial thickness and pattern

Patients were routinely followed up starting Day 7 of stimulation, with monitoring of follicle development performed using transvaginal ultrasound. An HCG trigger was given once 3 or more follicles reached ≥17 mm, ensuring adequate follicular development. If this criterion was not met, patients were observed every other day until triggering.

Endometrial Thickness Evaluation: On the day of HCG administration, endometrial thickness was assessed in the midsagittal plane of the uterine body. Measurement was performed by trained sonographers and senior physicians, adhering to standardized protocols for accuracy.

Endometrial Pattern Assessment: The endometrial pattern was classified into three groups based on echogenicity:

- A (Homogeneous echogenic): The endometrium exhibited a hyperechoic appearance, appearing brighter in grayscale, without distinct central echogenic lines.
- B (Triple line pattern): A multilayered endometrium showing prominent outer and central hyperechogenic lines with darker hypo-echoic regions in between.
- C (Heterogeneous echogenic): A mixed appearance of hyperechoic and hypoechoic patterns within the endometrium.

Each assessment was conducted with a focus on ensuring accurate categorization, facilitated by shared experiences among sonographers and clinical consultants.

3-6- Outcomes

Implantation rate defined as positive pregnancy test 14-day post embryo transfer. Live birth rate defined as the birth of one alive neonate after completion of 24 weeks of gestation.

3-7- Statistical analysis

Statistical analyses were conducted utilizing the R programming environment (R Core Team, 2014). Figures were generated using the ggplot2 package (Wickham, 2009), a powerful visualization tool within R.

Data Analysis Methods:

- Normally Distributed Data: Analyzed through t-tests for comparing means and one-way analysis of variance (ANOVA) for assessing differences among groups.
- Categorical Data: Analyzed using Pearson's chi-squared test, which identifies associations between categorical variables.
- A threshold of p-value < 0.05 was established for statistical significance, allowing for conclusions regarding the relationships between endometrial thickness, pattern, and reproductive outcomes.

Data Handling and Software Utilization:

Data integrity checks were thoroughly conducted prior to analysis, ensuring accurate interpretations. The software's capabilities allowed for complex modeling of outcomes based on the aforementioned characteristics, providing robust statistical insights.

4- Result

4-1- Demographic and Clinical Characteristics Results

In this study, a total of 301 IVF/ICSI cycles were analyzed to evaluate the correlation between endometrial characteristics and reproductive outcomes. Overall implantation rate was recorded at 44.1%, indicating the success of embryo implantation during the cycles studied. The demographic and clinical characteristics of the study population are summarized in Table 1. The maternal age of the participants ranged from 18 to 39 years, with a mean age of 29 ± 4.24 years. The endometrial thickness on the day of HCG administration varied from 6 mm to 17 mm, with a mean thickness of 1.06 ± 0.2 mm.

A significant aspect of the results is the distribution of stimulation protocols used across the cycles. The **long stimulation protocol** was employed in **63.73%** of the cases, while the **antagonist protocol** was utilized in **35.22%**. These protocols are designed to maximize ovarian response and enhance the chances of successful oocyte retrieval and embryo development.

The average duration of stimulation across the cycles was **12.2 ± 2.13 days**, indicating a relatively standard timeframe for optimal ovarian stimulation. On average, embryo transfer occurred on **Day 15.47 ± 2.03** of the cycle, which is consistent with typical practices in assisted reproductive technologies to allow for adequate follicular development and hormonal preparation of the endometrium.

Analyzing the underlying causes of infertility among participants provided further insights into the population characteristics. Infertility attributed to male factors was the most prevalent, accounting for 52.49% of cases. This was followed by anovulation at 13.29% and multiple factors at 25.25%. Other less common causes included poor ovarian reserve (0.33%), tubal factor (0.664%), endometriosis (0.33%), and unexplained infertility at 7.64%.

These results underscore the diverse range of factors contributing to infertility within the study population and highlight the complexity of managing such cases in a clinical setting. Variations in endometrial thickness, hormonal levels, and the specific underlying causes of infertility can significantly influence implantation rates and, ultimately, the success rates of IVF/ICSI cycles. Understanding these variables is vital for tailoring treatment approaches and improving overall reproductive outcomes.

Table 1 baseline cycle characteristics (N=301)

Variable	Mean ± SD
Maternal age (years)	29±4.24
Parity	1.46±1.04
BMI	26.1±3.36
Baseline FSH	7.26±7.33
Baseline E_2	88.5±77.8
Duration of stimulation(days)	12.30±2.13
Total dose of gonadotrophin (IU)	1973.27±3583.35
Endometrial thickness (mm)	1.06±0.2
E_2 on HCG Day	6452.8±3272.15
P on HCG Day (ng/ml)	1.4±1.8
No of oocyte retrieved	12.7±6.0
No. of embryo transferred	2.02±0.35
Stimulation protocol	
Long	63.73%
antagonist	35.22%
Total days of stimulation	12.2±2.13
Day of cycle ET occurred	15.47±2.03
Cause of infertility	
Male	52.49%
Anovulation	13.29%
Poor ovarian reserve	0.33%
Tubal	0.664%
Endometriosis	0.33%
Unexplained	7.64%
Multiple	25.25%

P=serum progesterone concentration

E_2= serum estradiol concentration

4-2- Endometrial pattern

In this analysis, the endometrial patterns observed in the subjects revealed that the majority, specifically 74.1%, exhibited a C pattern endometrium. This pattern is characterized by a mixed echogenic appearance on ultrasound, containing both hypo- and hyper-echogenic regions. The significance of endometrial patterns is well-documented in reproductive medicine, as they can provide insights into the receptivity of the endometrium and its potential impact on implantation success.

The distribution of endometrial patterns across two different thickness groups is illustrated in Figure 2. Despite varying patterns, the data indicated no statistically significant difference in pregnancy rates among the different endometrial patterns. Specifically, the pregnancy rate for pattern C was 45.74%, while it was 40.28% for pattern B and 33.33% for pattern A. The observed p-value was greater than 0.05, suggesting that endometrial pattern alone does not influence pregnancy outcomes in this cohort. These findings highlight an important aspect of IVF/ICSI cycles: while endometrial appearance can vary significantly among patients, it may not solely determine the likelihood of achieving pregnancy. Further investigation into complementary factors that influence endometrial receptivity and implantation success is warranted, particularly as we consider the intricate interplay between ultrasound findings and hormonal environments in reproductive cycles.

4-3- Endometrial thickness

Numerous studies have documented a positive correlation between endometrial thickness and IVF/ICSI success rates, prompting a thorough evaluation of this relationship within the current study. To assess this correlation, subjects were divided into two distinct groups based on endometrial thickness measurements: Group 1, consisting of participants with endometrial thickness below 8 mm, and Group 2, encompassing those with thickness equal to or greater than 8 mm.

Outcomes for the IVF/ICSI cycles were systematically analyzed for each group, and rates of pregnancy were calculated accordingly for each endometrial thickness interval. The analysis revealed a statistically significant positive correlation between pregnancy rates and endometrial thickness across all observed patterns. The p-value for this correlation was found to be less than 0.05, indicating a substantial link between thicker endometrial linings and higher pregnancy rates.

To further elucidate the dynamics of this relationship, a linear regression analysis was performed. The analysis demonstrated that endometrial thickness significantly influences clinical pregnancy rates, confirming the findings from prior literature. As shown in Figure 3, there is a robust positive linear correlation between endometrial thickness and pregnancy outcomes, with an R^2 value of 0.65. This value suggests that approximately 65% of the variability in pregnancy rates could be explained by variations in endometrial thickness.

Interestingly, the results indicated that while increasing endometrial thickness to 12 mm was associated with higher pregnancy rates, outcomes began to decline beyond this point. Specifically, the pregnancy rate in Group 2 (with thickness above or equal to 8 mm) was recorded at 45.26%, significantly higher than the 25% observed in Group 1 (with thickness below 8 mm). This finding underscores the importance of maintaining an optimal endometrial environment for enhancing reproductive success.

To provide a more comprehensive understanding of reproductive outcomes concerning varying endometrial thickness, we also evaluated key outcomes, including chemical pregnancies, clinical pregnancies, abortions, and live birth rates at each millimeter of endometrial thickness as summarized in

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Table 2.

The data revealed incremental increases in pregnancy rates as endometrial thickness increased, particularly for measurements up to 12 mm. However, as thickness exceeded this measurement, a decrement in pregnancy rates was noted, highlighting a potential threshold beyond which the endometrium may not favor implantation as effectively.

For example, in thickness intervals of 8 mm to 10 mm, pregnancy rates showed significant increases, reinforcing the notion that an optimal range exists for endometrial thickness. Conversely, while some factors may affect outcomes beyond thickness—such as hormonal balance and the timing of embryo transfer—it is essential for practitioners to monitor and optimize endometrial receptivity based on thickness measurements.

Further analysis of the data also indicated that chemical pregnancy rates, which represent early miscarriages following implantation, began to increase beyond certain thickness levels, while clinical pregnancy rates and live birth rates illustrated a similar trend in alignment with the observed endometrial measurements.

The combined data illuminate the critical role of endometrial thickness as a predictor of IVF success, emphasizing the need for individualized treatment plans that consider both structural and hormonal factors influencing endometrial health. Overall, this section underscores the complexity of assessing endometrial characteristics and their implications for fertility treatments. The findings provide a foundation for further prospective studies aimed at refining treatment strategies to enhance endometrial receptivity and improve overall IVF/ICSI outcomes, especially for patients navigating infertility challenges. The positive correlation between endometrial thickness and pregnancy rates should encourage clinicians to adopt a more nuanced approach in evaluating endometrial health to optimize reproductive success in assisted reproduction techniques.

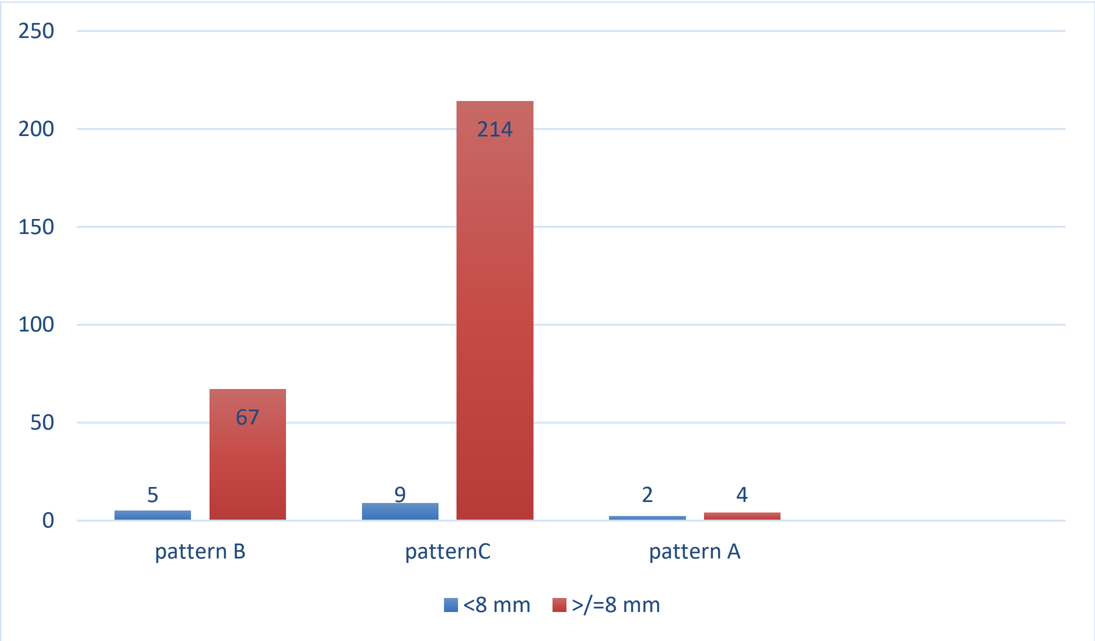

Figure 2. Distribution of endometrial pattern in two endometrial thickness groups

Endometrial Thickness	Cycle(n)	Pregnant (n)	Non pregnant(n)	Miscarriage (n)	chemical(n)	ectopic(n)	preterm delivery(n)	term delivery(n)
6-7	7	1	6	0	1	0	0	0
7-8	9	3	6	0	3	0	0	0
8-9	30	18	12	2	5	0	1	10
9-10	48	19	29	3	1	1	2	12
10-11	46	21	25	5	4	0	1	10
11-12	69	30	39	4	6	0	8	12
12-13	47	18	29	3	5	0	4	7
13-14	26	16	10	1	2	0	3	10
14-15	7	3	4	0	1	0	0	2
15-16	6	2	4	2	0	0	0	0
16-17	5	2	3	0	1	0	1	0
17-18	1	0	1	0	0	0	0	0
Sum	301	133(44.19%)	168(55.81%)	20(15.03%)	29(21.80%)	1	20(15.03%)	63(47.37%)

Table (2): Pregnancy outcome and endometrial thickness

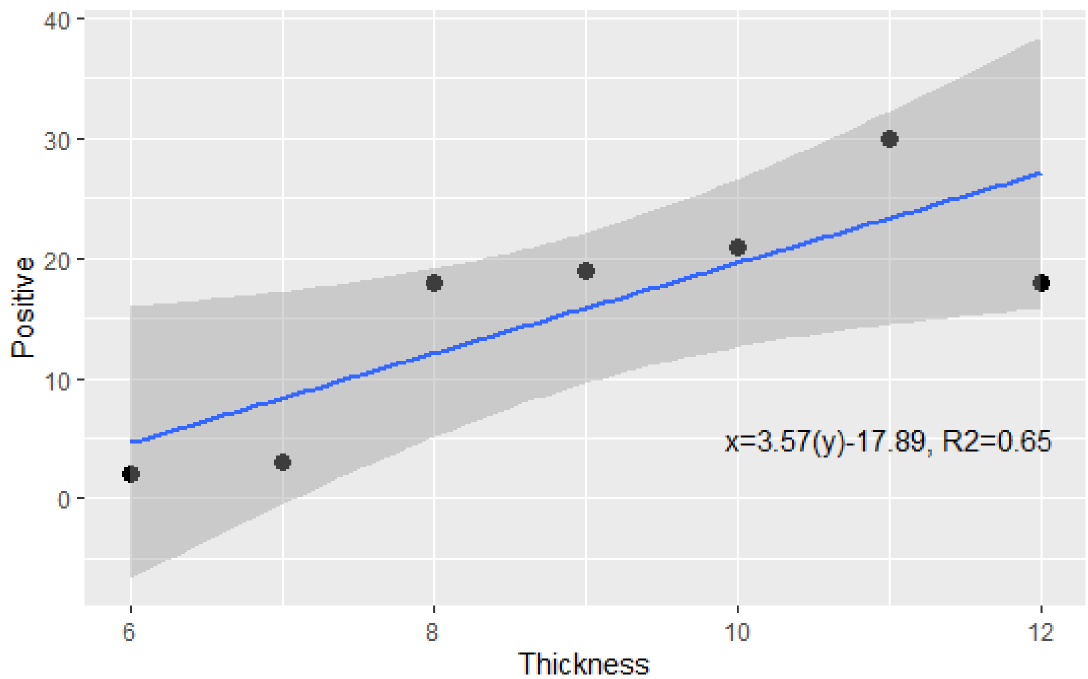

Figure (3). Linear regression between endometrial thickness and positive pregnancy test

LBR per cycle occurred only with group 2 and was higher with endometrial thickness 11-12mm (24.1%), one patient had tubal ectopic pregnancy which was treated by methotrexate endometrial thickness at HCG Day was 9 mm. another patient also gets pregnant but early pregnancy ultrasound showed multiple fetal anomalies and the pregnancy was terminated. No significant association between endometrial thickness and miscarriage.

5- DISCUSSION

The current study provides valuable insights into the relationship between endometrial characteristics and reproductive outcomes in IVF/ICSI cycles. Our findings confirm a positive correlation between endometrial thickness and live birth rates (LBR) when the endometrial thickness (EMT) is **8 mm or thicker**. Additionally, we observed that the endometrial pattern significantly impacted reproductive outcomes, independent of endometrial thickness. Notably, higher clinical pregnancy rates and LBR were recorded when endometrial thickness exceeded **11 mm**, with a plateau observed beyond this point, followed by a decline in outcomes when thickness surpassed **14 mm**. These results align with previous research that has explored similar correlations, reinforcing the importance of both endometrial thickness and pattern in predicting IVF success.

The positive correlation between endometrial thickness and reproductive outcomes has been a focal point in reproductive medicine. Numerous studies have demonstrated that an optimal endometrial thickness is crucial for successful implantation. Specifically, our findings suggest that while a thickness of **8 mm** is necessary for improved outcomes, a thickness above **11 mm** appears to enhance pregnancy rates further. This observation is consistent with the meta-analysis conducted by Kasius et al. (2014), which reported a significant increase in live birth rates with thicker endometrial linings. However, it is essential to note that this meta-analysis did not establish endometrial thickness as a definitive predictor of IVF/ICSI outcomes or as a reliable criterion for deciding between fresh and frozen embryo transfers. This ambiguity underscores the complexity of reproductive success, which is influenced by multiple factors beyond mere anatomical measurements.

Similarly, studies by Griesinger et al. (2018) and Ribeiro et al. (2018) corroborated our findings, emphasizing the negative impact of endometrial thickness less than **8 mm** on LBR and neonatal outcomes. These studies collectively highlight the critical threshold of **8 mm** as a minimum requirement for a favorable reproductive prognosis. Conversely, some research has failed to establish a positive relationship between endometrial thickness and reproductive outcomes, suggesting that while thickness is an important factor, it may not be the sole determinant of success in IVF/ICSI cycles.

Interestingly, Wang et al. (2018) proposed that the position of embryo transfer, when combined with endometrial thickness greater than **7 mm**, can enhance cycle outcomes. This finding suggests that procedural factors, alongside anatomical characteristics, play a significant role in the success of embryo implantation. The interplay between the timing of embryo transfer, the method of transfer, and the quality of the endometrium warrants further investigation to optimize IVF protocols.

Despite the strengths of our study, we acknowledge several limitations that could impact the generalizability of our findings. One significant limitation is the study design, which is retrospective in nature. Retrospective studies can introduce biases related to data collection and participant selection, potentially affecting the validity of the results. Additionally, the relatively small sample size limits the statistical power of our analysis and may hinder the ability to detect subtle differences in outcomes across different endometrial thickness and pattern groups.

Another limitation is the unequal distribution of participants between the two endometrial thickness groups. This imbalance may be attributed to the limited population available for the study, which could skew the results and affect the overall conclusions drawn regarding the relationship between endometrial characteristics and IVF/ICSI outcomes. Future studies should aim to recruit larger and more balanced populations to enhance the robustness of the findings.

Despite these limitations, our study's strengths lie in its ability to control for confounding variables such as maternal age and body mass index (BMI). By accounting for these factors, we can better isolate the effects of endometrial thickness and pattern on reproductive outcomes. Furthermore, all participants in our study had no history of uterine surgery, which is known to negatively affect endometrial growth and receptivity. This controlled environment strengthens the validity of our conclusions regarding the relationship between endometrial characteristics and IVF success.

In light of our findings and the existing literature, we recommend that future studies should focus on increasing sample sizes to further elucidate the predictive effects of endometrial thickness and pattern on IVF/ICSI outcomes. Larger studies may provide more definitive answers regarding the optimal endometrial thickness for successful implantation and the role of endometrial patterns in reproductive success. Additionally, prospective studies that examine the effects of various embryo transfer techniques, timing, and the influence of hormonal treatments on endometrial receptivity would further enrich our understanding of the factors influencing IVF outcomes.

Moreover, it is essential to explore the biological mechanisms underlying the observed associations between endometrial thickness, pattern, and reproductive outcomes. Understanding the histological and molecular characteristics of the endometrium at different thickness levels could provide valuable insights into why certain thicknesses are more favorable for implantation. Investigating factors such as endometrial receptivity markers, cytokine profiles, and the expression of adhesion molecules could help clarify the complex interplay between endometrial characteristics and reproductive success.

Our study reinforces the importance of endometrial thickness and pattern as significant factors influencing IVF/ICSI outcomes. The data suggest that maintaining an endometrial thickness of at least **8 mm**, with optimal outcomes observed at **11 mm**, is crucial for enhancing live birth rates. Additionally, the endometrial pattern appears to play a significant role in reproductive success, independent of thickness. While our findings contribute to the ongoing discourse on the relevance of endometrial characteristics in fertility treatments, further research is needed to address the limitations identified and to explore the underlying mechanisms that govern endometrial receptivity. By advancing our understanding of these factors, we can continue to improve the success rates of IVF/ICSI and provide better care for individuals and couples facing infertility challenges.

6- Conclusion & Recommendations

The results of the current study underscore the significance of both endometrial thickness and pattern in predicting reproductive outcomes in IVF/ICSI treatments. Our findings reveal a positive correlation between endometrial thickness and live birth rates (LBR), particularly when the thickness is **8 mm or greater**. Notably, we observed that optimal outcomes, including higher clinical pregnancy rates and LBR, were associated with endometrial thickness exceeding **11 mm**. However, thickness beyond **14 mm** showed a decline in outcomes, indicating a potential threshold effect. Additionally, the endometrial pattern demonstrated an independent association with reproductive success, suggesting that both the morphological appearance of the endometrium and its thickness play crucial roles in the success of IVF/ICSI cycles.

These findings align with the existing body of literature, which highlights the importance of the endometrium for successful implantation. While many studies have established a connection between endometrial thickness and reproductive outcomes, our research adds to this understanding by confirming these relationships within a carefully controlled patient population. However, it is important to recognize limitations, including the study's retrospective design, small sample size, and unequal distribution between groups, which may impact the generalizability of our results.

Recommendations

Based on the findings of this study, we propose several recommendations for clinical practice and future research that may enhance the effectiveness of IVF/ICSI cycles and deepen our understanding of endometrial characteristics:

1. Clinicians should consider tailoring IVF/ICSI protocols based on endometrial thickness measurements. Ensuring that the endometrial thickness is maintained at **8 mm or more** before embryo transfer could improve pregnancy rates. Those with thickness exceeding **11 mm** may be prioritized for embryo transfer, as this configuration appears to be associated with optimal outcomes. Regular monitoring of endometrial thickness via ultrasound during the stimulation phase is essential to make informed decisions regarding timing and method of embryo transfer.

2. The endometrial pattern, particularly the presence of a C pattern, should be included in routine evaluations for patients undergoing IVF/ICSI. Given that endometrial pattern may significantly influence reproductive outcomes independent of thickness, it would be prudent to consider both metrics when assessing a patient's readiness for embryo transfer.

3. Future studies should aim to confirm and refine the optimal endometrial thickness for IVF success. Larger prospective studies with more balanced participant distributions are needed to validate the threshold effects observed in our study, particularly around the nuanced relationships between thickness levels (e.g., beyond **14 mm**) and reproductive outcomes. Additionally, researchers should explore the histological features of the endometrium at various thickness levels to elucidate the biological basis for these correlations.

4. Future investigations should incorporate the study of endometrial receptivity markers at varying thicknesses. Identifying molecular or biochemical markers of receptivity could provide a more comprehensive understanding of why certain endometrial characteristics favor successful implantation. Researchers could examine factors such as cytokine profiles, hormone levels, and gene expression in the endometrium to enhance our understanding of the complexities surrounding endometrial receptivity.

5. Research should also focus on the impact of different embryo transfer techniques and their interaction with endometrial characteristics. Studies that analyze the effect of transfer timing, transfer positions, and embryo handling on implantation success in relation to endometrial measurements could offer valuable insights into optimizing protocols.

6. Clinicians should educate patients about the importance of endometrial thickness and pattern to foster better understanding and communication regarding treatment decisions. Patients who are

informed about the significance of these factors may be more engaged and active participants in their care, potentially leading to improved comfort and adherence to treatment protocols.

7. It could be beneficial to conduct longitudinal studies to assess how endometrial characteristics affect long-term reproductive health post-IVF/ICSI. Understanding the longer-term implications of varying endometrial thickness and patterns could be crucial for informing clinical practice and enhancing overall patient outcomes.

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