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The Impact of Endometrial Thickness on Pregnancy Rates in Women Undergoing IVF with Donor Oocytes: Implications for Public Health Action

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Abstract

The impact of endometrial thickness on pregnancy rates in women undergoing IVF with donor oocytes has significant implications for public health. Successful implantation during in vitro fertilization (IVF) is crucially dependent on both a healthy endometrium and a viable blastocyst. The measurement of endometrial thickness (EMT) via ultrasound scan has emerged as a non-invasive means to evaluate endometrial receptivity. Nonetheless, its significance in clinical practice for women using donor oocytes remains unclear. This study aims to examine how endometrial thickness influences pregnancy outcomes in women undergoing IVF with donor oocytes in Makurdi, with the goal of providing valuable insights for public health action. We conducted a cross-sectional study involving 265 women who underwent IVF and embryo transfer using donor oocytes. Participants were divided into three groups based on their EMT: Group 1 (EMT < 7 mm), Group 2 (EMT between 7 - 14 mm), and Group 3 (EMT > 14 mm). Key demographic and clinical data—including age, height, weight, number of oocytes transferred, and pregnancy rates—were gathered and analyzed using SPSS version 25.0. Statistical methods included Student's t-test for continuous variables, Pearson's Chi-square (χ^2) test for categorical data, logistic regression to control for confounding factors, and Receiver Operating Characteristic (ROC) curve analysis to evaluate the predictive value of EMT. The average age of participants was 42.4 years, with chemical and clinical pregnancy rates recorded at 75.5% and 53.6%, respectively. Notable findings include a significant association between age and clinical pregnancy rates ($p = 0.008$). While other factors such as parity, BMI, previous IVF cycles, hormone treatments, and embryo grading did not show a significant relationship with pregnancy outcomes but endometrial thickness demonstrated a significant correlation ($p = 0.000$). Specifically, pregnancy rates were lower for women with EMT < 7.0 mm (37.3%) compared to those with EMT between 7 - 14 mm (49.0%) and > 14 mm (51.7%). Logistic regression confirmed that age-adjusted EMT significantly impacts pregnancy outcomes. ROC curve analysis revealed an area under the curve (AUC) of 0.63, with an EMT cut-off value of 8.0 mm providing a sensitivity of 75.4% and a specificity of 48.8%. These findings highlight the significant influence of endometrial thickness on clinical pregnancy rates in IVF cycles using donor oocytes. While increased EMT correlates with improved outcomes, its overall predictive accuracy is limited. The results advocate for personalized approaches in IVF treatment protocols, emphasizing informed decision-making among healthcare providers and patients. Recognizing the importance of endometrial thickness in reproductive health can inform public health initiatives aimed at enhancing awareness of IVF practices among potential candidates, tailoring IVF treatments based on individual patient profiles, and promoting research into factors affecting endometrial receptivity. Ultimately, these efforts can lead to improved pregnancy rates and reproductive success in assisted reproductive technologies.

Keywords: Endometrial thickness, In-vitro fertilization, Oocyte donation, Pregnancy rates, public health.

INTRODUCTION

In vitro fertilization (IVF) has been a leading method for treating infertility since its introduction in 1978. In Nigeria, approximately 19.2% of couples experiencing infertility may require IVF, highlighting its significance as a public health concern. The IVF process involves extracting eggs from the ovaries, incubating, and inseminating them for 18-20 hours. Following confirmation of fertilization, the embryos are cultured for about 36 hours before being transferred back to the uterus. Over four decades, pregnancy rates per IVF cycle have varied from 8.6% to 46.2%, with a clinical pregnancy rate of 30% reported in Nigeria.

Several factors influence IVF success, with maternal age being a critical predictor, alongside the morphological quality of embryos. Additionally, endometrial characteristics, including thickness and quality, are vital for implantation. The endometrium is essential for embryo implantation, which marks the beginning of pregnancy. Endometrial thickness varies during the menstrual cycle, ranging from 2-4 mm during the menstrual phase to up to 16 mm in the secretory phase.

Implantation involves three phases: apposition, where the blastocyst loosely adheres to the endometrial surface; attachment, which is characterized by strong adhesion facilitated by paracrine signaling; and penetration, where the embryo invades the endometrial epithelium and establishes a vascular connection with the mother. The clinical significance of endometrial thickness remains debated. While a thin endometrium is linked to lower conception and higher abortion rates, excessive thickness has also been implicated in poor implantation success, and there is no universally accepted definition for what constitutes a "thin" endometrium.

In oocyte donation, the controlled environment allows for the examination of endometrial receptivity and its effects on pregnancy success, particularly in cases where traditional IVF has failed. Improved understanding of the relationship between endometrial thickness and IVF outcomes can lead to better educational resources and enhanced public awareness regarding the importance of endometrial health in achieving successful IVF outcomes.

The number and quality of embryos transferred play significant roles in influencing the success rates of in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI). The rates of pregnancy and multiple pregnancies depend on the implantation rate and the number of embryos transferred. Limiting the number of embryos transferred to one or two can enhance uterine receptivity and improve embryo quality.

To address gaps in existing literature, this proposed study is designed to collect accurate and complete data while minimizing recall and misclassification biases. The study will exclude women with a history of uterine pathologies to reduce confounding factors that might impact the results. Additionally, the quality of embryos will be thoroughly assessed, ensuring that only high-quality embryos are transferred to maximize the chances of success. These methodological measures will enhance the validity and reliability of the study, providing valuable insights into outcomes related to oocyte donation.

The justification for this research lies in providing evidence-based information on the clinical significance of endometrial thickness (EMT) for women undergoing IVF using donor oocytes. As IVF is a common assisted reproductive technology (ART) for infertile couples, its success hinges on both embryo quality and endometrial receptivity. EMT measurement is a non-invasive and widely accepted approach for assessing endometrial receptivity during IVF treatment. However, existing literature shows conflicting results regarding EMT's impact on IVF outcomes. While some studies indicate that thin EMT negatively affects pregnancy rates, others do not find such a correlation. Consequently, there is no definitive conclusion on EMT's role in conception probability, especially among women using donor oocytes. This study aims to elucidate the relationship between EMT and pregnancy outcomes in this specific population, helping clinicians define optimal EMT thresholds for improved IVF results. Ultimately, this could enhance public and familial satisfaction related to pregnancy and childbirth.

Aim: The aim of this study is to investigate the effect of endometrial thickness on the clinical pregnancy rate in women undergoing IVF-ET using donor oocytes in Makurdi, with a focus on its population and public health implications.

The objectives include:

1. To assess the association between endometrial thickness (measured in millimeters) and pregnancy rates confirmed by ultrasound in women undergoing IVF-ET with donor oocytes.
2. To evaluate the diagnostic accuracy of endometrial thickness as a predictor of pregnancy confirmed by ultrasound in women receiving donor oocytes.
3. To provide recommendations based on these findings that can inform policy development with culturally acceptable public health considerations.

The hypotheses for this research are as follows:

- **Null Hypothesis (H0):** There is no association between endometrial thickness and pregnancy

rates in women undergoing IVF-ET using donor oocytes.

- **Alternate Hypothesis (Ha):** There is an association between endometrial thickness and pregnancy rates in women undergoing IVF-ET using donor oocytes.

METHODOLOGY/METHODS

Study Setting: This study was conducted at Foundation Memorial Hospital in Makurdi, Benue State, a private medical center known for its assisted reproductive technology (ART) services. The hospital serves as a referral center for advanced infertility management (IVF/ICSI), diagnostic endoscopic gynecological surgeries, antenatal care, management of high-risk pregnancies, high-resolution ultrasonography, and general gynecology. From August 2018 to June 2021, more than 1,400 patients have undergone a total of 20 ART cycles, with an average of 70 participants per cycle. The patients are typically grouped in cycles that occur bi-monthly, resulting in six ART cycles per year.

Study Design: This research employs a cross-sectional analytical study design focused on pregnancy rates in women undergoing IVF-ET using donor oocytes.

Study Population: Eligible women who consented and met the inclusion criteria were recruited for the study.
Study Period: The study commenced following ethical approval from the management of Foundation Hospital Makurdi and ran from May 2023 to February 2024.

Inclusion Criteria: Participants included women aged 18 to 45 years, who underwent IVF/embryo transfer using donor oocytes, and who consented to participate in the study.

Exclusion Criteria: Women were excluded if they had a history of uterine surgery, uterine abnormalities, recurrent miscarriages, endometrial hyperplasia or cancer, uterine fibroids, or any medical conditions affecting endometrial thickness measurement.

Sample Size Determination: The minimum sample size was calculated using Fisher's formula: [N = \frac{Z^2pq}{d^2}]
Where:
Z = 1.96 (95% confidence interval)
p = 0.192 (prevalence of infertility requiring IVF)
q = 1 - p = 0.808
d = 0.05 (degree of accuracy)
Placing in these values: [N = \frac{(1.96^2 \times 0.192 \times 0.808)}{0.05^2} = 238] To account for a 10% non-response rate, the sample size was adjusted: [N_s = \frac{N}{1 - f}]
Where (f=0.1) (10%non-responserate), yielding: [N_s = \frac{238}{0.9} = 265] Thus, a total of 265 women were recruited for the study.

Sampling Method: A convenience sampling method was used, recruiting every consecutive woman who met the eligibility criteria until the sample size was achieved.

PROCEDURES

Oocyte Donors: Oocyte donors, aged 23–30 years, were women with proven fertility. They underwent thorough counseling about the medical and legal aspects of egg donation, including risks, benefits, emotional impacts, and the legal implications of their participation. After counseling, donors signed informed consent forms and underwent routine screening for infections and other tests before starting the treatment cycle.

Downregulation and Ovarian Stimulation: Baseline hormone levels (LH, FSH, and estradiol) were assessed on day 2 or 3 of the cycle, followed by a transvaginal scan. The long protocol for down-regulation involved administering 0.5 mg of buserelin daily, tapering down to 0.25 mg before stimulation with recombinant FSH.

Oocyte Retrieval: Conducted via transvaginal ultrasound-guided aspiration 36 hours post-hCG administration. The aspirated follicular fluid was processed to isolate oocytes for fertilization.

Sperm Collection and Preparation: Semen was collected on the day of oocyte retrieval and processed through a washing technique to prepare a high-quality sperm sample.

In Vitro Fertilization: Oocytes were inseminated with prepared sperm, and fertilization was confirmed by observing two pronuclei after 18-20 hours. Embryos were then assessed for quality based on cleavage and morphology.

Recruitment of Study Participants: Eligible patients undergoing IVF using donor oocytes were identified and counseled about the study. They received detailed information, signed informed consent, and completed a structured proforma regarding their demographic data. The treatment cycles were conducted in batches to efficiently utilize resources.

Recipients' Preparation: Recipients with normal menstrual cycles received medications for synchronization to optimize uterine receptivity leading up to embryo transfer.

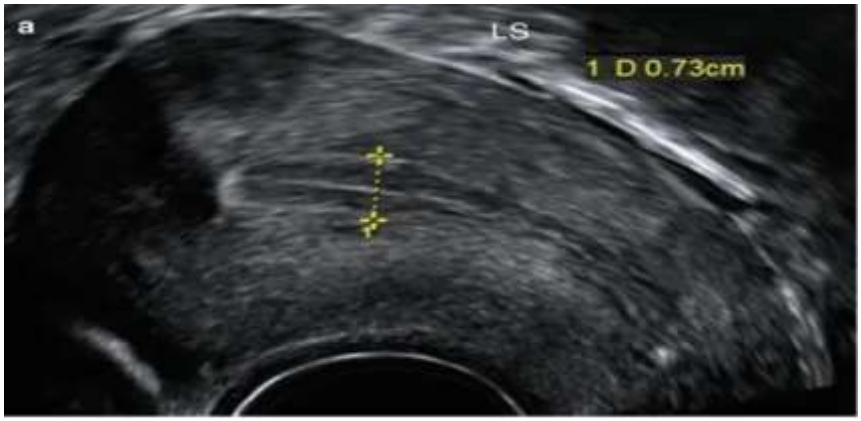


Figure 1: Measurement of Endometrial Thickness Using Transvaginal Ultrasonography

Outcome Measure: The primary outcome measure for this study was the clinical pregnancy rate, assessed both per cycle and per transfer, as demonstrated by ultrasonography. A serum pregnancy test was conducted two weeks after embryo transfer (ET), followed by a transvaginal ultrasound performed four to five weeks after a positive β-hCG test result. Clinical pregnancy was defined by the visualization of a gestational sac with a detectable fetal heartbeat. Biochemical pregnancy was identified by an initial rise and subsequent fall in serum β-hCG levels without any sonographic confirmation. A miscarriage was defined as a pregnancy loss occurring before gestational week 20 after the visualization of an intrauterine gestational sac at 5 to 6 weeks of gestation.

Data Analysis: Data on patient demographics, including age, height, weight, number of oocytes transferred, endometrial thickness, and clinical pregnancy rates, were collected and analyzed using SPSS version 25.0 (IBM® SPSS Statistics Inc., Armonk, New York, USA). Continuous variables were presented as mean ± standard deviation (SD) and assessed using Student's t-test. Categorical data were expressed as frequencies and analyzed using Pearson's Chi-square (χ^2) test, with a significance level set at $P < 0.05$. Logistic regression was employed to evaluate the independent effects of individual variables on clinical pregnancy outcomes, and results were presented in tabular format.

Ethical Approval: Ethical approval for the study (FMH/FMC/HREC/108/Vol.1/x) was obtained from the health research ethics committee of the FMC, Makurdi. Participants provided written informed consent prior to enrollment and were informed of their right to withdraw from the study at any time. The study ensured participant privacy, with all information treated confidentially.

RESULTS

Table 1 presents the basic characteristics of the participants, with a mean age of 42.4 ± 5.1 years. Among the 265 participants, 200 (75.5%) achieved a biochemical pregnancy, and 142 (53.6%) achieved a clinical pregnancy. The mean age of participants who achieved clinical pregnancy was 41.6 years (SD = 5.0), compared to 43.2 years (SD = 5.1) for those who did not, with this age difference being statistically significant (p = 0.008). In terms of parity, there were 90 nulliparous participants (54.9%) among those who achieved clinical pregnancy, compared to 74 (45.1%) among those who did not, but the difference in parity was not statistically significant (p = 0.384). The mean BMI for participants achieving clinical pregnancy was 41.6 kg/m² (SD = 5.0), while for those who did not, it was 42.4 kg/m² (SD = 5.1), with no significant difference observed (p = 0.601). Most participants in both groups had undergone two or fewer previous IVF cycles, and there was no significant difference in the number of previous cycles between the two groups (p = 0.402). Furthermore, the distribution of participants undergoing hormonal treatment also showed no significant difference between those achieving clinical pregnancy and those who did not (p = 0.237), nor did the number of embryos transferred (p = 0.122) or the embryo grading (4AB vs. 4BB) (p = 0.298). Table 2 outlines the distribution of endometrial thickness, revealing that participants with thickness less than 7.0 mm had a lower clinical pregnancy rate (37.3%) compared to those with thickness between 7 - 14 mm (49.0%) and greater than 14 mm (51.7%), with the differences being statistically significant (p = 0.000). Table 3 summarizes logistic regression analysis showing that endometrial thickness significantly affects clinical pregnancy outcomes (p = 0.000), even when adjusted for age. Figure 1 presents a Receiver Operating Characteristic (ROC) curve analysis, indicating an Area Under the Curve (AUC) of 0.63 for endometrial thickness predicting clinical pregnancy in IVF-ET cycles with donor oocytes, with a threshold of 8.0 mm yielding a sensitivity of 75.4% and a specificity of 48.8%.

Table 1: Basic Characteristics of Participants

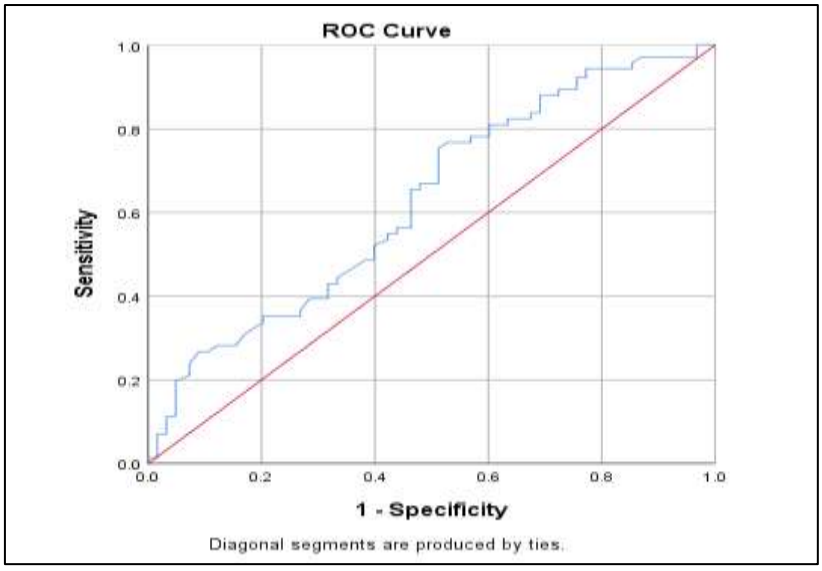
Variables	Clinical Pregnancy		*Test Statistic*	P-value
	Yes 142 (53.6%)	No 123 (46.4%)		
Age (years) Mean±SD	41.6±5.0	43.2±5.1	0.1	0.008
Parity N (%)				
Nullipara	90 (54.9)	74 (45.1)	3.1	0.384
Para 1	35 (49.3)	36 (50.7)		
Para 2	10 (71.4)	4 (28.6)		
Para 3	7 (43.8)	9 (56.3)		
BMI (Kg/m^2) Mean±SD	41.6±5.0	42.4±5.1	5.3	0.601
Previous IVF cycles N (%)			**2.9**	**0.402**
None	65 (56.0)	51 (44.0)		
One	33 (54.1)	28 (45.9)		
Two	36 (54.5)	30 (45.5)		
≥ Three	8 (36.4)	14 (63.6)		
Hormonal treatment			**1.4**	**0.237**
Cycling	125 (55.1)	102 (44.9)		
Non-cycling	17 (44.7)	21 (55.3)		
Number of embryos transferred N (%)			**4.2**	**0.122**
Two	47 (63.5)	27 (36.5)		
Three	52 (51.0)	50 (49.0)		
Four	43 (48.3)	46 (51.7)		
Embryo grading N (%)			**1.1**	**0.298**
4AB	8 (42.1)	11 (57.9)		
4BB	134 (54.5)	112 (45.5)		

Table 2: Association Between Endometrial Thickness and Clinical Pregnancy Rate in IVF-ET Cycles with Donor Oocytes

Endometrial thickness	Clinical Pregnancy		X^2	P-value
	Yes	No		
< 7.0 mm	19 (37.3)	32 (62.7)	17.1	0.000
7 - 14 mm;	50 (49.0)	52 (51.0)		
> 14 mm	46 (51.7)	43 (48.3)		

Table 3: Age-Adjusted Logistic Regression Analysis on The Influence of Endometrial Thickness on Clinical Pregnancy Rate in IVF-ET Cycles with Donor Oocytes

Variables	Coef (B)	S.E.	Odds Ratio (Exp B)	95% CI Lower	95% CI Upper	P-value
Age (years)	0.06	0.03	1.06	1.0	1.1	0.024
Endometrial thickness	-0.82	0.22	0.44	0.3	0.7	0.000



AUC = 0.63

Figure 2: Receiver Operating Characteristic (ROC) Curve Demonstrating the Predictive Value of Endometrial Thickness for Clinical Pregnancy in IVF-ET Cycles with Donor Oocytes

DISCUSSION

This cross-sectional analytical study investigated the effect of endometrial thickness on clinical pregnancy rates in women undergoing IVF-ET with donor oocytes. The overall biochemical and clinical pregnancy rates reported were 75.5% and 53.6%, respectively, with the clinical rate slightly lower than that observed by Noyes *et al*. at 63% but higher than Arce *et al*.'s 42.3%. Variations in treatment protocols, laboratory techniques, and embryo transfer criteria could account for these discrepancies. Notably, participants with endometrial thickness less than 7.0 mm had a significantly lower clinical pregnancy rate (37.3%) compared to those with thickness between 7 - 14 mm (49.0%) and greater than 14 mm (51.7%), reinforcing findings from earlier studies by Okohue *et al*. and Aydin *et al*., which similarly reported better pregnancy outcomes associated with thicker endometrial measurements. However, our findings contrasted with Dian et al. and Arce *et al*., who found no significant differences, likely arising from differences in study design and patient populations. The study emphasized that optimal endometrial thickness is essential for embryo implantation because it reflects the uterine lining's receptivity and structural integrity, crucial for providing nutrients and oxygen to the embryo. Additionally, a statistically significant difference was observed in the mean age of participants achieving clinical pregnancy (41.6 years) compared to those who did not (43.2 years), consistent with other studies highlighting younger age as a favorable factor. Parity, BMI, number of previous IVF cycles, type of hormonal treatment, and embryo grading did not significantly differ between groups, in line with findings from Rashidi et al. and Arce *et al*. Although these factors did not correlate with clinical pregnancy rates, they may influence other outcomes, such as live birth rates, with studies indicating that higher BMI negatively impacts clinical pregnancy rates and increases the risk of complications. The quality of embryos was found to be critical for IVF success; while our study's results did not show significant associations, other studies have confirmed its importance.

In analyzing the predictive power of endometrial thickness using a Receiver Operating Characteristic (ROC) curve, an AUC of 0.63 suggested moderate discriminatory capability, with a cutoff value of 8.0 mm correlating with improved clinical pregnancy rates. However, this AUC also indicates that endometrial thickness alone is not a strong predictor of success. Some literature, including Zhao *et al*. and Kasius *et al*., has questioned the relevance of endometrial thickness in predicting IVF outcomes, suggesting that it may have limited value in decision-making regarding treatment progress. Contrary to our null hypothesized association between endometrial thickness and pregnancy rates, statistical analyses demonstrated a significant relationship, leading to the rejection of the null hypothesis. This research thus supports the notion that endometrial thickness is an important factor in clinical pregnancy outcomes for women undergoing IVF-ET with donor oocytes.

This study's strengths include a comprehensive evaluation of the impact of endometrial thickness on pregnancy rates within a specific population and the incorporation of age adjustment to minimize confounding effects. The cross-sectional design helped eliminate recall bias and issues related to loss to follow-up. However, limitations such as potential biases in patient selection may affect the generalizability of the findings. Furthermore, while our study established an association between endometrial thickness and clinical pregnancy rates, it does not imply causation, as this relationship may be influenced by other factors affecting endometrial receptivity, such as blood flow or underlying physiological mechanisms. Finally, the inability to assess the influence of certain confounding factors on live birth rates highlights the need for further longitudinal research to draw more definitive conclusions.

CONCLUSION

Endometrial thickness significantly influences clinical pregnancy rates in IVF-ET cycles using donor oocytes, with distinct success rates observed across various thickness categories. While our findings are consistent with previous research highlighting the benefits of optimal endometrial thickness for achieving higher pregnancy rates, discrepancies may arise from differences in study designs and patient demographics. Although the cutoff value of 8.0 mm shows predictive value, its moderate discriminatory power indicates that reliance solely on endometrial thickness as a predictive tool is insufficient, necessitating careful interpretation during clinical decision-making.

RECOMMENDATIONS

To enhance public health outcomes, we recommend the following: First, while endometrial thickness is a valuable prognostic indicator, patient management should be individualized, incorporating a range of factors rather than relying exclusively on EMT measurement. Second, future studies should adopt prospective designs involving larger and more diverse cohorts to validate findings and comprehensively address potential confounders. Also, integrating multi-dimensional assessments, such as evaluating endometrial vascular patterns and utilizing biomarkers of uterine receptivity, could significantly improve predictive models and ultimately enhance IVF-ET outcomes.

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