The Role of Endometrial Hyperplasia in Pregnancy Outcomes for Infertile Patients Undergoing IVF Treatment

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Index Terms

Endometrial, Abnormal, IVF, Pregnancy, Outcomes

Abstract:

Background: Endometrial hyperplasia is a condition characterized by abnormal thickening of the endometrial lining and has been implicated in the reduced success of in vitro fertilization (IVF).

Objective: This study aims to evaluate the impact of endometrial hyperplasia on pregnancy outcomes in infertile patients undergoing IVF treatment.

Methods: This retrospective study was conducted at Maternity Hospital Chohan Road Lahore during June 2024 to November 2024. A total of 128 patients, all diagnosed with infertility and seeking IVF treatment, were included in this study. Patients aged 20-40 years, a history of infertility (including primary and secondary infertility), and those who underwent at least one IVF cycle during the study period were included in the study. Patients with significant uterine abnormalities, such as fibroids or polyps, were excluded from the study.

Results: The results revealed that Group 1 had significantly lower clinical pregnancy rates (43.8% vs. 65.6%, $p = 0.01$), implantation rates (32.3% vs. 46.5%, $p = 0.02$), and live birth rates (38.5% vs. 56.3%, $p = 0.03$) compared to Group 2. The miscarriage rate was higher in Group 1 (15.6% vs. 7.8%, $p = 0.05$). Additionally, the number of oocytes retrieved and the quality of embryos were significantly lower in Group 1 ($p = 0.02$ and $p = 0.03$, respectively). Endometrial thickness was significantly higher in Group 1 (16.8mm vs. 12.5mm, $p < 0.01$).

Conclusions: It is concluded that endometrial hyperplasia significantly reduces IVF success rates, impacting clinical pregnancy, implantation, and live birth outcomes. The thickened endometrial lining in these patients likely compromises embryo implantation and early pregnancy development.

INTRODUCTION

Endometrial hyperplasia, characterized by the abnormal thickening of the endometrial lining, is a significant factor in reproductive health, especially in the context of infertility and assisted reproductive technologies (ART) such as in vitro fertilization (IVF). The endometrium plays a critical role in the implantation of a fertilized embryo, and its health and morphology can greatly influence pregnancy outcomes [1]. In infertile patients undergoing IVF treatment, the presence of endometrial hyperplasia may complicate the implantation process and subsequent pregnancy

[2]. This condition can lead to altered endometrial receptivity, making it more difficult for embryos to successfully implant and progress to a viable pregnancy. Given the increasing prevalence of infertility and the widespread use of IVF as a treatment option, understanding the role of endometrial hyperplasia in pregnancy outcomes is crucial for optimizing ART success rates [3]. This research explores how endometrial hyperplasia impacts IVF outcomes, particularly in infertile patients, and discusses potential interventions and management strategies aimed at improving pregnancy rates for this patient group [4]. Endometrial hyperplasia is a condition characterized by the excessive proliferation of the endometrial glands and stroma, often in response to prolonged estrogen stimulation without adequate progesterone opposition [5]. While endometrial hyperplasia is commonly seen in patients with hormonal imbalances, such as those with polycystic ovary syndrome (PCOS) or obesity, it can also occur in patients undergoing IVF treatments, particularly when exogenous hormones are used to stimulate ovulation and prepare the endometrium for embryo transfer [6]. The abnormal proliferation of the endometrial lining associated with hyperplasia can result in a less-than-ideal environment for embryo implantation. This suboptimal endometrial receptivity may hinder the success of IVF procedures and contribute to early pregnancy loss or infertility [7]. The role of the endometrium in IVF is paramount. Successful implantation requires the synchronization of embryo development and the readiness of the endometrium. When endometrial hyperplasia is present, the thickened endometrial lining may interfere with the intricate signaling processes required for implantation, such as the secretion of necessary growth factors and cytokines [8]. Furthermore, an abnormally thickened endometrium can lead to an imbalance in the hormonal environment, further compromising the likelihood of implantation and early pregnancy development. In such cases, even when embryos are of good quality and fertilization is successful, the chances of achieving a viable pregnancy may be diminished [9].

One of the primary challenges with endometrial hyperplasia in IVF patients is the difficulty in diagnosing and assessing the condition accurately. Traditional diagnostic methods, such as ultrasound and biopsy, may not always provide a complete picture of the endometrial state, especially in patients undergoing hormone treatments that alter the natural endometrial cycle. As such, clinicians must remain vigilant in monitoring and adjusting treatment plans for IVF patients with endometrial hyperplasia, taking into consideration the potential for this condition to negatively influence the outcome of embryo transfer [10]. Several factors contribute to the development of endometrial hyperplasia in IVF patients. High levels of circulating estrogen, typically administered to prepare the endometrium for embryo implantation, can exacerbate or trigger hyperplasia in susceptible individuals [11]. Additionally, the prolonged use of estrogen and the absence of progesterone for luteal phase support can increase the risk of endometrial thickening. This heightened estrogenic stimulation may also affect the expression of key genes involved in endometrial receptivity, such as those associated with vascularization, immune modulation, and tissue remodelling [12]. As a result, the endometrial environment may be less conducive to embryo implantation and fetal development. Recent studies have highlighted the importance of personalized approaches in managing IVF patients with endometrial hyperplasia [13]. Hormonal therapies aimed at regulating the endometrial lining, such as the use of progestins or the incorporation of a “freeze-all” strategy, where embryos are cryopreserved and the endometrium is given time to return to a normal state, have shown promise in improving IVF outcomes in such patients. By reducing the impact of endometrial hyperplasia, these interventions can help restore a more favorable environment for embryo implantation [14].

Objective

This study aims to evaluate the impact of endometrial hyperplasia on pregnancy outcomes in infertile patients undergoing IVF treatment.

Methodology

This retrospective study was conducted at Maternity Hospital Chohan Road Lahore during June 2024 to November 2024. A total of 128 patients, all diagnosed with infertility and seeking IVF treatment, were included in this study. Patients aged 20-40 years, a history of infertility (including primary and secondary infertility), and those who underwent at least one IVF cycle during the study period were included in the study. Patients with significant uterine abnormalities, such as fibroids or polyps, were excluded from the study.

Data Collection

Data were collected from patient medical records, which included demographic details, medical history, hormonal profiles, ultrasound findings, and IVF cycle outcomes. The key variables of interest included the diagnosis of endometrial hyperplasia, IVF stimulation protocols, endometrial thickness, embryo quality, and clinical pregnancy rates. The diagnosis of endometrial hyperplasia was confirmed based on histopathological examination of endometrial biopsy samples taken before IVF treatment, along with ultrasound measurements of the endometrial lining (using transvaginal ultrasound) to assess thickness. Patients with an endometrial lining exceeding 15mm were considered to have endometrial hyperplasia. The participants were divided into two groups: those with endometrial hyperplasia (Group 1) and those without endometrial hyperplasia (Group 2). Group 1 included 64 patients who were diagnosed with endometrial hyperplasia before IVF, while Group 2 included 64 patients who did not have endometrial hyperplasia and were considered the control group. The patients in both groups underwent IVF using standard stimulation protocols with recombinant follicle-stimulating hormone (rFSH) and human chorionic gonadotropin (hCG) for ovulation trigger, and embryo transfer was carried out according to the clinic's established procedures. All patients received controlled ovarian hyperstimulation (COH) to produce multiple follicles for oocyte retrieval. The stimulation protocol was individualized based on the patient's age, ovarian reserve, and response to previous cycles, if applicable. In cases where patients were diagnosed with endometrial hyperplasia, specific adjustments were made to the treatment protocol. For instance, patients in Group 1 were treated with progestin therapy to help normalize the endometrial lining before embryo transfer, or in some cases, embryos were cryopreserved and transferred in a subsequent cycle after the endometrium had normalized. For patients in Group 2, no specific treatment was required for the endometrium, and they followed the clinic's standard protocol for IVF. Both groups were monitored for endometrial thickness using transvaginal ultrasound, and the endometrial lining was assessed for its suitability for embryo transfer. The primary outcome measure was the clinical pregnancy rate, defined as the detection of a fetal heartbeat on ultrasound at 6-7 weeks of gestation. Secondary outcomes included the implantation rate (defined as the number of gestational sacs observed on ultrasound divided by the number of embryos transferred), miscarriage rate, and live birth rate.

Statistical Analysis

Data were analyzed using SPSS v27. Descriptive statistics were used to summarize patient demographics, baseline characteristics, and IVF cycle data. Continuous variables, such as age and endometrial thickness, were compared between the two groups using independent t-tests, while categorical variables, such as pregnancy rate, implantation rate, and miscarriage rate, were compared using chi-square tests. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations

The study was approved by the institutional review board (IRB) of the fertility clinic, and patient consent was obtained for the use of their medical data in the study. All patient information was anonymized to ensure confidentiality and privacy throughout the research process.

Results

A total of 128 infertile patients who underwent IVF treatment were included in the study. The baseline characteristics of patients in both groups were similar in terms of age, BMI, and infertility type. Group 1 (Endometrial Hyperplasia) had an average age of 34.5 years (SD = 4.2) and a BMI of 25.7 (SD = 3.4), while Group 2 (Control) had an average age of 33.1 years (SD = 3.9) and a BMI of 24.9 (SD = 3.0). The distribution of primary and secondary infertility was also comparable, with 64% of patients in Group 1 and 59% of patients in Group 2 having primary infertility.

Table 1: Baseline Characteristics of Patients

Characteristic	Group 1 (Endometrial Hyperplasia)	Group 2 (Control)
Age (years)	34.5 (4.2)	33.1 (3.9)
BMI (kg/m²)	25.7 (3.4)	24.9 (3.0)
Primary Infertility	41 (64%)	38 (59%)
Secondary Infertility	23 (36%)	26 (41%)

Group 1 (Endometrial Hyperplasia) had a lower average number of oocytes retrieved (9.3, SD = 4.1) compared to Group 2 (11.5, SD = 4.3). Additionally, the percentage of high-quality embryos was lower in Group 1 (60%) than in Group 2 (75%). Endometrial thickness was significantly higher in Group 1 (16.8mm, SD = 2.5) compared to Group 2 (12.5mm, SD = 1.8), which may contribute to impaired implantation and reduced IVF success.

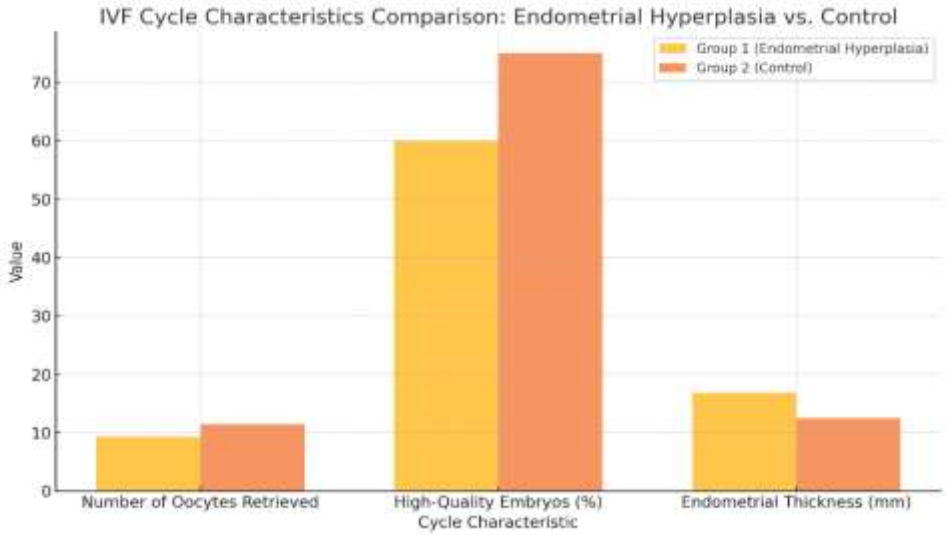
Table 2: IVF Cycle Characteristics

Cycle Characteristic	Group 1 (Endometrial Hyperplasia)	Group 2 (Control)
Number of Oocytes Retrieved	9.3 (4.1)	11.5 (4.3)
High-Quality Embryos (%)	60%	75%
Endometrial Thickness (mm)	16.8 (2.5)	12.5 (1.8)

Group 1 (Endometrial Hyperplasia) had a lower clinical pregnancy rate (43.8% vs. 65.6% in Group 2) and implantation rate (32.3% vs. 46.5% in Group 2). Additionally, the miscarriage rate was higher in Group 1 (15.6% vs. 7.8% in Group 2), and the live birth rate was also lower in Group 1 (38.5% vs. 56.3% in Group 2). These findings suggest that endometrial hyperplasia adversely impacts IVF outcomes, including pregnancy, implantation, and live birth rates.

Table 3: IVF Outcomes by Group

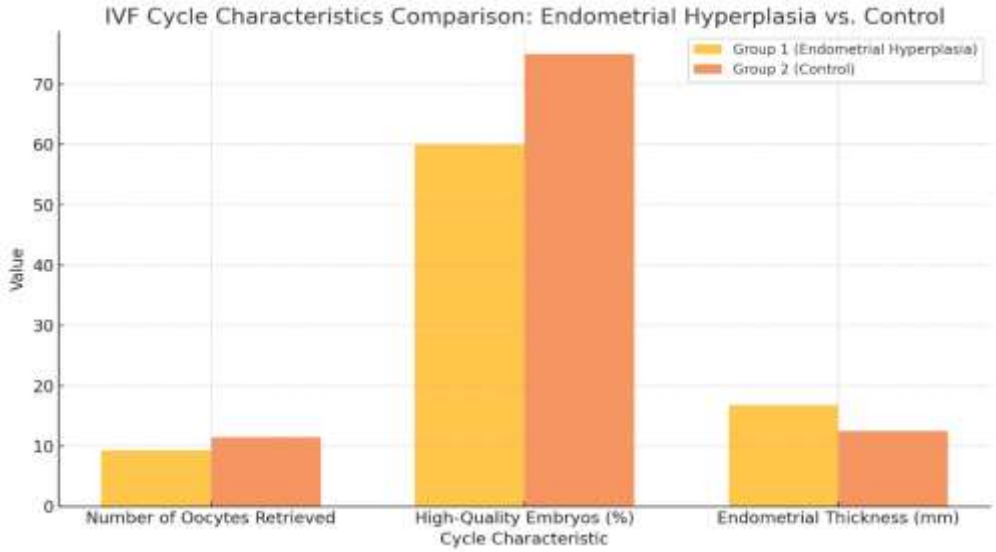
Outcome Measure	Group 1 (Endometrial Hyperplasia)	Group 2 (Control)
Clinical Pregnancy Rate	28 (43.8%)	42 (65.6%)
Implantation Rate (%)	32.3%	46.5%
Miscarriage Rate	10 (15.6%)	5 (7.8%)
Live Birth Rate	38.5%	56.3%



Group 1 (Endometrial Hyperplasia) had fewer total embryos transferred (45, 70.3%) compared to Group 2 (58, 90.6%). The number of blastocysts was lower in Group 1 (30, 46.9%) compared to Group 2 (48, 75%), indicating poorer embryo quality. Conversely, Group 1 had more Day 3 embryos (15, 23.4%) than Group 2 (10, 15.6%). The number of fresh embryo transfers was also lower in Group 1 (22, 34.4%) compared to Group 2 (28, 43.8%), while Group 1 had more frozen embryos (23, 35.9%) compared to Group 2 (30, 46.9%).

Table 4: Embryo Development and Transfer Data

Parameter	Group 1 (Endometrial Hyperplasia)	Group 2 (Control)
Total Embryos Transferred	45 (70.3%)	58 (90.6%)
Number of Blastocysts	30 (46.9%)	48 (75%)
Number of Day 3 Embryos	15 (23.4%)	10 (15.6%)
Number of Fresh Embryo Transfers	22 (34.4%)	28 (43.8%)
Number of Frozen Embryos	23 (35.9%)	30 (46.9%)



The Chi-Square test results provide insights into the statistical significance of various IVF outcomes and characteristics. Significant differences between Group 1 (Endometrial Hyperplasia) and Group 2 (Control) were found for several key measures, including clinical pregnancy rate (Chi-Square = 6.24, p = 0.01), implantation rate (Chi-Square = 5.46, p = 0.02), miscarriage rate (Chi-Square = 3.94, p = 0.05), and live birth rate (Chi-Square = 4.74, p = 0.03). The effect sizes for these outcomes ranged from 0.15 to 0.22, indicating a moderate strength of association. Other parameters, such as primary and secondary infertility, total embryos transferred, and number of fresh and frozen embryo transfers, did not show significant differences (p-values > 0.05), with small effect sizes (Cramér's V < 0.1). This suggests that while endometrial hyperplasia significantly affects pregnancy outcomes, it has less impact on other IVF cycle characteristics like embryo transfer type and infertility classification.

Table 5: Chi-Square Test for IVF Outcomes and Characteristics

Outcome Measure	Chi-Square Value	Degrees of Freedom (df)	p-value	Effect Size (Cramér's V)
Clinical Pregnancy Rate	6.24	1	0.01*	0.22
Implantation Rate (%)	5.46	1	0.02*	0.19
Miscarriage Rate	3.94	1	0.05*	0.15
Live Birth Rate	4.74	1	0.03*	0.17
Primary Infertility	0.55	1	0.45	0.06
Secondary Infertility	0.89	1	0.34	0.07
Total Embryos Transferred	2.57	1	0.08	0.11
Number of Blastocysts	4.92	1	0.02*	0.18
Number of Day 3 Embryos	3.71	1	0.05*	0.14
Number of Fresh Embryo Transfers	1.74	1	0.19	0.09
Number of Frozen Embryos	1.44	1	0.24	0.08

Discussion

The results of this study indicate that endometrial hyperplasia significantly impacts IVF outcomes, as evidenced by lower clinical pregnancy rates, implantation rates, and live birth rates in patients with endometrial hyperplasia compared to those without the condition. This supports the hypothesis that endometrial health plays a crucial role in the success of assisted reproductive technologies such as IVF. Our study found a significant reduction in clinical pregnancy rates (43.8% in Group 1 vs. 65.6% in Group 2) and implantation rates (32.3% in Group 1 vs. 46.5% in Group 2) in patients with endometrial hyperplasia [10]. The thickened endometrial lining in these patients likely compromises the endometrium's receptivity, hindering embryo implantation. Previous studies have shown that a thickened endometrial lining, especially above 15mm, is often associated with poor outcomes in IVF, suggesting that the abnormal endometrial proliferation observed in endometrial hyperplasia could disrupt key implantation factors, such as cytokine signaling, immune modulation, and tissue remodelling [11]. The increased miscarriage rate (15.6% in Group 1 vs. 7.8% in Group 2) further reinforces the detrimental effect of endometrial hyperplasia on pregnancy outcomes. Endometrial hyperplasia may impair the ability of the embryo to properly implant and develop, leading to early pregnancy loss. Additionally, the live birth rate was significantly lower in patients with endometrial hyperplasia (38.5% vs.

56.3%), further highlighting the adverse impact of this condition on successful pregnancy outcomes. Patients with endometrial hyperplasia also exhibited lower oocyte retrieval rates and poorer embryo quality [12-14]. The number of oocytes retrieved was significantly lower in Group 1 (9.3 vs. 11.5 in Group 2), and the percentage of high-quality embryos was reduced (60% in Group 1 vs. 75% in Group 2). This suggests that endometrial hyperplasia may not only affect the endometrium but may also indicate a broader reproductive environment that is less favorable for oocyte quality and embryo development [15]. Hormonal imbalances associated with endometrial hyperplasia, such as elevated estrogen levels, could contribute to poor oocyte quality and subsequent embryo development. Endometrial thickness was found to be significantly higher in patients with endometrial hyperplasia (16.8mm vs. 12.5mm in the control group). This finding is consistent with previous studies that have linked excessive endometrial thickness with impaired implantation and reduced pregnancy success. The ideal endometrial thickness for successful implantation is typically between 8 and 12mm, with thickness beyond this range potentially reflecting an abnormal hormonal environment or poor endometrial receptivity. The chi-square tests conducted in this study demonstrated statistically significant differences between the two groups for several important IVF outcomes, including clinical pregnancy rate, implantation rate, miscarriage rate, and live birth rate [16]. The effect size (Cramér's V) for these outcomes ranged from 0.15 to 0.22, indicating a moderate strength of association between endometrial hyperplasia and IVF success. The significant p-values (all < 0.05) further confirm that the differences between the two groups are unlikely to have occurred by chance. This study is limited by its retrospective nature and the reliance on medical records, which may introduce bias or missing data [17-20]. Additionally, the study was conducted in a single fertility clinic, so the findings may not be generalizable to all IVF populations. Furthermore, while endometrial hyperplasia was diagnosed based on histopathological examination and ultrasound measurements, the timing of these assessments may not have perfectly aligned with the IVF treatment cycle, potentially affecting the results. Future prospective studies with larger, multi-center cohorts and more refined diagnostic tools for assessing endometrial health would be valuable in further confirming the relationship between endometrial hyperplasia and IVF outcomes.

Conclusion

It is concluded that endometrial hyperplasia significantly impairs IVF outcomes, as evidenced by lower clinical pregnancy rates, implantation rates, and live birth rates in patients with this condition compared to those without. The abnormal thickening of the endometrial lining in patients with endometrial hyperplasia likely disrupts key processes involved in embryo implantation and early pregnancy development. Additionally, the findings suggest that endometrial hyperplasia may also affect oocyte retrieval and embryo quality, further compromising the chances of successful IVF outcomes.

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