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ORIGINAL ARTICLE

Biochemical and Anatomical Predictors of Endometrial Receptivity in IVF Patients with Haematological Disorders

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ABSTRACT

Background: Women suffering from disorders of the blood have specific difficulties with 'implantation in the context of in vitro fertilization (IVF)' because of vascular or hormonal system challenges. Gaining insight into what impacts endometrial receptivity in this population may assist in formulating optimized approaches for their management.To evaluate the biochemical and anatomical predictors of endometrial receptivity and their association with IVF outcomes in women with haematological conditions.

Methods: This observational study took place at Hayatabad Medical Complex, Peshawar, from January 2021 to January 2022. It included 79 women with different types of blood disorders who were undergoing IVF treatment. Each participant was evaluated for endometrial receptivity using ultrasound contouring ,including assessment of the endometrium's thickness, its pattern, vascularity plus hormonal Prole (estradiol, progesterone, TSH, and prolactin). The outcomes of IVF showed fertilization rates along with 'emerging embryo quality as well as their implantation and live birth rates that there were differences between receptive and non-receptive groups'.

Results: Patients with receptive endometrium were significantly younger and had a shorter duration of infertility. Higher levels of estradiol and progesterone and lower TSH and prolactin were associated with receptivity. Sonographic parameters including greater endometrial thickness, trilaminar pattern, and enhanced vascular flow strongly correlated with successful implantation and live birth. Clinical pregnancy and live birth rates were significantly higher in the receptive group ($p< 0.05$).

Conclusion: Endometrial receptivity in IVF patients with haematological disorders is closely linked to specific hormonal and anatomical markers. Incorporating these assessments into routine IVF protocols can enhance treatment success and guide individualized care.

Keywords: Endometrial Receptivity; In Vitro Fertilization; Haematological Disorders; Estradiol; Endometrial Thickness; Doppler Ultrasound; IVF Outcomes

INTRODUCTION

The attainment of in 'vitro fertilization procedures (IVF) is dependent on a myriad factors, including the quality of embryos, as well as the functionality of the endometrium in facilitating implantation, a component known as endometrial receptivity'. Women suffering from haematological disorders such as thalassemia, chronic anemia, or even thrombophilia may face negative impacts on reproductive outcomes due to systemic inflammation and chronically modified medication regimens alongside changes in blood flow to the uterus. These conditions are rather insidious; they progressively optimize the uterine milieu even in the absence of conspicuous symptoms leading to failure in implantation despite good-quality embryo transfers[1-3].

Despite advances in reproductive medicine improving the success of IVF procedures, the importance of endometrial health within this particular patient population continues to be overlooked. Estradiol and progesterone, alongside other biochemical markers, play essential roles in supporting the sequential advancement of the endometrium; thyroid hormones and prolactin also impact broader aspects of reproductive physiology. Concurrently, ultrasound examinations focusing on endometrial thickness, its echogenic pattern, and associated vascularization have proven valuable as non-invasive methods for measuring receptivity[4-6].

Previous studies have primarily focused on women with normal reproductive profiles, often excluding those with systemic or chronic illnesses[7-9]. However, women with haematological disorders represent a growing proportion of fertility patients, and tailored evaluation is essential to optimize their chances of conception. This study was designed to assess the key biochemical and anatomical indicators of endometrial receptivity in this unique group and to explore how these markers relate to IVF success. By identifying reliable predictors, clinicians may better individualize care and improve outcomes in women with complex reproductive backgrounds.

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METHODOLOGY

The observational study took place in the Department of Obstetrics and Gynecology at Hayatabad Medical Complex, Peshawar, from January 2021 to January 2022. It focused on assessing the 'biochemical and anatomical predictors of endometrial receptivity in women with known haematological disorders undergoing in vitro fertilization (IVF)'. Ethical approval was granted by the review board of Hayatabad Medical Complex which allowed collection of data. All participants provided informed written consent.

A total of 79 female patients were enrolled through consecutive sampling. All participants were between 20 and 40 years of age, diagnosed with a haematological disorder (such as thalassemia, thrombophilia, or other coagulopathies), and scheduled for IVF treatment. Women with known uterine anomalies, endometriosis, or chronic medical conditions unrelated to their haematological status that could affect endometrial development were excluded.

Before initiating the IVF cycle, detailed clinical histories were obtained, and physical examinations were performed. Baseline investigations included transvaginal ultrasonography to assess uterine anatomy and endometrial baseline thickness, as well as routine blood tests to evaluate endocrine and metabolic status. Hormonal profiles, including FSH, LH, estradiol, progesterone, AMH, TSH, and prolactin, were measured using standard immunoassay techniques. These tests were performed on day 2–3 of the menstrual cycle and repeated, where relevant, on the day of ovulation trigger or embryo transfer.

Endometrial assessment was carried out on the day of ovulation trigger using transvaginal ultrasound, measuring endometrial thickness, pattern, and volume. Additionally, Doppler ultrasound was used to evaluate uterine artery resistance and pulsatility indices, as well as endometrial blood flow using Applebaum's vascular zone classification.

The IVF protocol was individualized but generally followed a gonadotropin-releasing hormone (GnRH) antagonist protocol, with ovulation triggered using recombinant hCG once leading follicles reached maturity. 'Embryo transfer was performed on day 3 or day 5, and endometrial receptivity was categorized based on ultrasound features and clinical response: an endometrial thickness of ≥8 mm, trilaminar pattern, and adequate vascularity (zones 3 or 4) were considered receptive'.

Outcomes assessed included fertilization rate, embryo quality, implantation rate, clinical pregnancy, and live birth rate. Data were stratified into two groups: those with receptive and non-receptive endometrium. Statistical analysis was carried out using SPSS software. Continuous variables were expressed as means with standard deviations, and categorical variables as frequencies and percentages. Independent t-tests and chi-square tests were used to compare groups, with a p-value of <0.05 considered statistically significant.

RESULTS

A total of 79 women undergoing IVF treatment with underlying haematological disorders were included in the analysis. Patients were divided into two groups based on endometrial receptivity: receptive (n = 45) and non-receptive (n = 34). The receptive group had a statistically lower mean age (31.6 ± 4.2 years) compared to the non-receptive group (33.1 ± 4.8 years, p = 0.048), indicating that younger women may have a more favorable endometrial response. Although the mean BMI was slightly lower in the receptive group, the difference was not statistically significant.

A significant association was found between 'shorter duration of infertility and endometrial receptivity (p = 0.041), suggesting that prolonged infertility may be linked to impaired endometrial conditions'. Smoking appeared more frequently among women in the non-receptive group (32.4% vs. 15.6%, p = 0.038), highlighting its negative impact on uterine health. Likewise, previous failed IVF cycles were more common among the non-receptive group (p = 0.023), pointing to repeated implantation failure potentially tied to receptivity issues. No significant differences were observed in the type of haematological disorder or in the prevalence of comorbidities such as hypertension or diabetes.

Table 1: Demographic and Clinical Characteristics of IVF Patients (n = 79)

Variable	Receptive (n = 45)	Non-Receptive (n = 34)	p-value
Mean Age (years)	31.6 ± 4.2	33.1 ± 4.8	0.048*
BMI (kg/m²)	24.9 ± 3.1	26.3 ± 3.5	0.062
Duration of infertility (years)	4.1 ± 2.3	5.2 ± 2.6	0.041*
Type of haematological disorder			
– Thalassemia	16 (35.6%)	12 (35.3%)	0.98
– Thrombophilia	21 (46.7%)	16 (47.1%)	
– Other	8 (17.7%)	6 (17.6%)	
Smoking status (yes)	7 (15.6%)	11 (32.4%)	0.038*
Comorbidities (HTN/DM)	9 (20.0%)	10 (29.4%)	0.33
Previous IVF attempts (≥1)	13 (28.9%)	18 (52.9%)	0.023*

Serum hormonal profiles revealed significant differences between the two groups. Estradiol levels were notably higher in women with receptive endometrium (2200 ± 410 pg/mL) compared to those with non-receptive lining (1905 ± 360 pg/mL, p = 0.011), reflecting a stronger ovarian response. Similarly, progesterone concentrations were significantly greater in the receptive group (p< 0.001), supporting optimal luteal function and embryo-endometrial synchrony.

Though FSH, LH, and AMH values did not show statistically meaningful variation, a trend favoring better ovarian reserve in the receptive group was observed. Importantly, 'TSH and prolactin levels were both significantly lower in the receptive group, with p-values of 0.016 and 0.049 respectively, suggesting subtle hormonal imbalances may impact receptivity even in euthyroid women'.

Table 2: Biochemical Predictors of Endometrial Receptivity

Biochemical Marker	Receptive (Mean ± SD)	Non-Receptive (Mean ± SD)	p-value
Estradiol (pg/mL)	2200 ± 410	1905 ± 360	0.011*
Progesterone (ng/mL)	12.5 ± 2.1	9.8 ± 2.4	<0.001*
FSH (mIU/mL)	6.9 ± 1.5	7.3 ± 1.7	0.29
LH (mIU/mL)	5.1 ± 1.3	4.7 ± 1.5	0.22
AMH (ng/mL)	2.4 ± 1.1	1.9 ± 1.2	0.072
TSH (μIU/mL)	2.0 ± 0.8	2.5 ± 0.9	0.016*
Prolactin (ng/mL)	19.4 ± 5.2	21.7 ± 4.8	0.049*

Endometrial anatomy showed clear distinctions between the groups. Women with receptive linings had significantly thicker endometria (9.8 ± 1.3 mm) compared to the non-receptive group (7.5 ± 1.1 mm, p< 0.001), underscoring the clinical value of ultrasound measurements on the day of trigger or transfer. A trilaminar endometrial pattern was more commonly observed in the receptive group (84.4% vs. 55.9%, p = 0.003), which has traditionally been associated with successful implantation.

Doppler assessments revealed lower uterine artery resistance in the receptive group (p< 0.001), suggesting better perfusion. Furthermore, a significantly higher proportion of women in the receptive group had blood flow reaching zones 3 and 4 of the endometrium (p = 0.002). Endometrial volume also favored the receptive group, reinforcing the multifactorial nature of receptivity.

Table 3: Anatomical and Ultrasound-Based Predictors

Anatomical Feature	Receptive (n = 45)	Non-Receptive (n = 34)	p-value
Endometrial thickness (mm)	9.8 ± 1.3	7.5 ± 1.1	<0.001*
Endometrial pattern (trilaminar)	38 (84.4%)	19 (55.9%)	0.003*
Uterine artery RI (mean)	0.61 ± 0.05	0.68 ± 0.07	<0.001*
Endometrial blood flow (zone 3/4)	32 (71.1%)	13 (38.2%)	0.002*
Endometrial volume (mL)	4.2 ± 1.1	3.1 ± 1.0	0.008*

The impact of endometrial receptivity was reflected in key IVF outcomes. Women with receptive endometrium had significantly higher fertilization rates (p = 0.005) and more good-quality embryos available for transfer (p = 0.007). Most notably, clinical pregnancy and live birth rates were significantly higher in this group (57.8% and 53.3%, respectively), compared to 26.5% and 20.6% in the non-receptive group.

Table 4: IVF Outcomes According to Endometrial Receptivity

Outcome	Receptive (n = 45)	Non-Receptive (n = 34)	p-value
Fertilization rate (%)	74.6 ± 8.5	66.8 ± 9.3	0.005*
Good-quality embryos (n ≥2)	36 (80.0%)	18 (52.9%)	0.007*
Clinical pregnancy rate (%)	26 (57.8%)	9 (26.5%)	0.003*
Implantation rate (%)	42.1 ± 10.3	28.4 ± 9.7	0.001*
Miscarriage rate (%)	4 (8.9%)	6 (17.6%)	0.18
Live birth rate (%)	24 (53.3%)	7 (20.6%)	0.002*

Implantation rate followed the same trend, showing a statistically superior outcome in the receptive cohort (p = 0.001). Although the miscarriage rate was higher in the non-receptive group, the difference did not reach statistical significance. Overall, the data strongly support the association between biochemical and

anatomical indicators of endometrial health and successful IVF outcomes in this high-risk population.

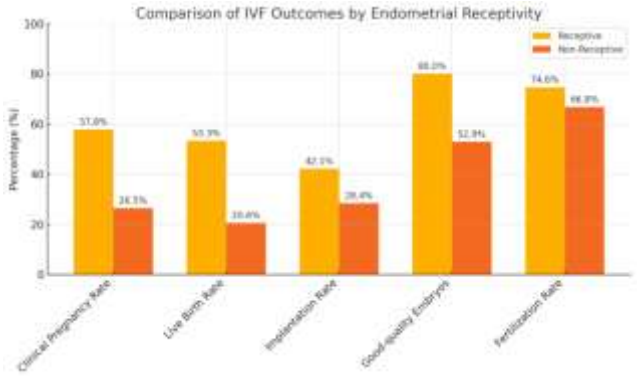

Figure 1: Graph showing the comparison of IVF outcomes between women with receptive and non-receptive endometrium.

DISCUSSION

Our study highlight the multifaceted nature of endometrial receptivity, particularly in women with underlying haematological disorders undergoing assisted reproductive treatment. Among the most prominent observations was the association between younger maternal age, shorter duration of infertility, and improved endometrial receptivity. These results were consistent with existing literature, which suggests that age-related changes in the uterine environment, vascularization, and hormonal responsiveness can negatively impact implantation potential. Similar studies who noted a gradual decline in endometrial receptivity markers with advancing maternal age, independent of ovarian reserve[10,11].

Importantly, smoking status and prior IVF failures emerged as significant negative predictors in this cohort. Smoking has been widely recognized for its vasoconstrictive and oxidative effects on the endometrium, and our findings reinforce this detrimental association. Additionally, women with multiple previous IVF attempts were more likely to have non-receptive endometrium, suggesting a possible underlying defect in the endometrial milieu or poor synchronization with embryo development[12-14].

In terms of biochemical predictors, the study demonstrated that higher estradiol and progesterone levels on the day of ovulation trigger were strongly associated with receptive endometrium. This is in agreement with the findings of studies that emphasized the importance of hormonal priming for adequate endometrial transformation[15,16]. Furthermore, women with receptive endometrium exhibited significantly lower TSH and prolactin levels, supporting the hypothesis that even subtle hormonal imbalances can interfere with uterine readiness. A study also identified elevated prolactin as a marker for poor implantation outcomes, consistent with our results[17,18].

From an anatomical perspective, endometrial thickness, trilaminar pattern, and adequate vascular perfusion (zones 3/4) were significantly associated with better IVF outcomes. These sonographic markers have long been regarded as reliable non-invasive indicators of uterine receptivity. Our study adds to the growing body of evidence by demonstrating that endometrial blood flow and volume are particularly relevant in patients with haematological conditions, who may already be at risk of impaired vascular dynamics due to chronic disease or anticoagulant therapy. The role of uterine artery resistance index (RI) as a predictor was also validated here, with lower RI correlating with higher pregnancy rates. These findings align with Doppler studies which similarly found a strong association between endometrial perfusion and embryo implantation[19,20].

The correlation between receptivity markers and IVF success rates was particularly striking. Women with receptive endometrium showed higher fertilization, implantation, and live birth rates compared to those with non-receptive linings. These outcomes confirm the critical role of the endometrial environment, not only in embryo acceptance but also in sustaining early pregnancy. While miscarriage rates were slightly higher in the non-receptive group, the difference was not statistically significant, possibly due to the small sample size or the presence of other confounding factors such as genetic embryo quality.

One limitation of this study is its observational design, which restricts the ability to draw causal inferences. Additionally, we did not assess molecular markers of receptivity such as integrins, HOXA10, or LIF expression, which could have provided more mechanistic insights. Nevertheless, the strength of this study lies in its focused population women with haematological disorders—who are often underrepresented in fertility research despite facing unique reproductive challenges.

CONCLUSION

This study reinforces the importance of both biochemical and anatomical parameters in evaluating endometrial receptivity among IVF patients with haematological disorders. Younger age, non-smoking status, favorable hormonal profiles, and optimal sonographic findings all contributed to higher clinical pregnancy and live birth rates. Careful assessment of these variables can guide individualized treatment plans and improve outcomes in this high-risk population. Incorporating routine ultrasound and hormonal monitoring into IVF protocols may serve as a practical and cost-effective approach to enhance embryo implantation and pregnancy success in women with systemic health challenges

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