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PHYSIOLOGICAL AND HORMONAL PREDICTORS OF IMPLANTATION SUCCESS IN WOMEN UNDERGOING OVULATION INDUCTION

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ABSTRACT
Background: The implantation process is extremely important during establishment of pregnancy, and can be influenced by maternal, ovarian, hormonal, follicular, and endometrial factors. Ovulation induction can be employed to enhance the chances of conception for women with infertility; however, successful ovulation does not always lead to implantation. The identification of reliable predictors may help to better counsel and plan patient treatment.
Objective: To evaluate physiological and hormonal predictors of implantation success in women undergoing ovulation induction.
Methods: A prospective observational study was conducted at Liaqat Memorial Hospital, Kohat, from April 2025 to October 2026. A total of 89 women who were undergoing ovulation induction were included. Demographic parameters, factors related to infertility, ovarian reserve markers, hormonal parameters, follicular development, endometrial parameters and treatment-related variables were recorded. The serum β-hCG was used to evaluate the success of the implantation after the induction cycle. The participants were divided into successful and unsuccessful implantation groups. Group comparisons were made with appropriate tests and multivariable binary logistic regression was used to determine independent predictors of implantation success. A p-value <0.05 was considered statistically significant.
Results: Successful implantation occurred in 36 women (40.4%)**,** while 53 (59.6%) had unsuccessful implantation. Women with successful implantation were younger and had lower BMI and shorter infertility duration. They also demonstrated significantly higher AMH, trigger-day estradiol, and mid-luteal progesterone levels, whereas baseline FSH was lower. Successful implantation was additionally associated with greater antral follicle count, larger dominant follicle diameter, a higher number of mature follicles, increased endometrial thickness, and a trilaminar endometrial pattern. On multivariable analysis, younger age, higher AMH, higher mid-luteal progesterone, larger dominant follicle diameter, and greater endometrial thickness remained significant independent predictors of successful implantation.
Conclusion: Implantation success following ovulation induction is influenced by multiple physiological and hormonal factors. Younger maternal age, favorable ovarian reserve, adequate luteal progesterone, appropriate follicular maturation, and greater endometrial thickness appear to be important predictors. Combined assessment of these parameters may assist in individualized fertility treatment and estimation of implantation probability.

KEYWORDS: Ovulation induction, implantation, infertility, AMH, progesterone, endometrial thickness, follicular development.

INTRODUCTION
Infertility is a significant reproductive health issue addressed by couples around the world and has significant emotional, social and financial implications. Common conditions which cause female infertility are ovulatory disorders, which can be caused by endocrine disorders, poly-cystic ovary, hypothalamic dys-function or by other changes in the reproductive physiology. Ovulation induction is thus a very common approach to stimulate development of the follicles and induce their development and ovulation in women who have irregular periods and in some women undergoing assisted conception. Induction of ovulation, however, does not necessarily lead to pregnancy

as successful conception involves the proper maturation of the oocytes, fertilization, development of the embryo, receptivity of the endometrium and subsequent implantation (1-3).
Implantation is a complex biological process, in which the developing embryo comes into contact and attaches to a receptive endometrium. It relies on the correct timing of the hormonal and physiological changes that occur in the peri-ovulatory and luteal phases of the menstrual cycle. Estrogen stimulates the proliferation of the endometrium and progesterone causes secretory changes and prepares the endometrium for embryo attachment. Normally, these hormone pathways are disturbed and consequently make it less likely for the implantation to take place even if the ovulation is successful (4, 5).
Several ovarian reserve and endocrine markers have been studied as potential prognosticators for reproductive outcome. AMH is a marker of ovarian reserve and is sometimes used to predict ovarian responsiveness to stimulation. Additional information about hypothalamic-pituitary-ovarian function is obtained by measuring the levels of follicle-stimulating hormone and luteinizing hormone. Concentrations of the hormone estradiol during follicular maturation are indicative of ovarian activity, while concentrations of the hormone progesterone during the mid-luteal phase are an indirect measure of ovulation and corpus luteum activity. The relationship between these hormonal variables could thus affect the optimization of implantation conditions (6-8).
Another important point to consider in treatment response evaluation is the ultrasonographic characteristics. During the cycle of ovulation induction, the size of the dominant follicle, the number of mature follicles, the number of antral follicles, endometrial thickness and endometrial pattern may be clinically useful. Optimum follicular maturation optimises the likelihood of releasing a good quality oocyte and sufficient endometrial development is required for embryo attachment. Even though the follicles grow well, it may be difficult to implant because of a thin or poorly developed endometrium (9).
Reproductive outcomes may also be affected by maternal characteristics. As age goes up, so does the decline in ovarian reserve, the quality of oocytes, and chromosomal abnormalities; and high BMI could be a factor affecting insulin sensitivity, ovarian steroidogenesis, inflammation, and endometrial function. The likelihood of becoming pregnant can also be influenced by the length of the infertility and the nature of the infertility. Thus, the implantation rate is likely to be influenced by a combination of demographic, physiological, hormonal, ovarian and endometrial factors and not by any one of these (10).
While many markers are evaluated in the course of the treatment of the patient with infertility, the contribution of each of these markers to the success of the implantation after induction of ovulation is still relevant for clinical purposes. Being able to identify predictors that will be available may enable clinicians to make better estimates of treatment prognosis, fine tuning of cycles monitoring, better counseling, and individualize treatment strategies. This is especially useful for everyday clinical practice where high-tech reproductive technologies are not always easily accessible.
The present study was therefore conducted to evaluate physiological and hormonal predictors of implantation success in women undergoing ovulation induction. It aimed to compare demographic, hormonal, follicular, and endometrial characteristics between women with successful and unsuccessful implantation and to identify independent factors associated with a favorable implantation outcome.

METHODOLOGY

This study was conducted at Liaqat Memorial Hospital, Kohat, from April 2025 to October 2026. A prospective observational study design was used to evaluate physiological and hormonal factors associated with implantation success among women undergoing ovulation induction. A total of 89 women who fulfilled the eligibility criteria were enrolled through non-probability consecutive sampling. The study focused on identifying demographic, ovarian, hormonal, follicular, and endometrial parameters that could predict successful implantation following ovulation induction.
Women of reproductive age undergoing ovulation induction for infertility treatment were considered eligible for inclusion. Participants with either primary or secondary infertility were included provided they were planned for an ovulation-induction cycle and completed the required hormonal and ultrasonographic assessment. Women with severe systemic illness, uncontrolled thyroid disease, hyperprolactinemia requiring active treatment, major uterine abnormalities, untreated pelvic pathology, premature ovarian insufficiency, or incomplete clinical records were excluded. Women who discontinued treatment before completion of the monitored cycle were also excluded from the final analysis.
After enrollment, detailed demographic and clinical information was recorded using a structured data collection proforma. Variables included age, body mass index, duration of infertility, type of infertility, previous fertility treatment, and relevant reproductive history. Baseline physiological parameters, including systolic and diastolic blood pressure and resting pulse rate, were documented. Body mass index was calculated as weight in kilograms divided by height in meters squared. The ovarian reserve assessment included serum anti-Müllerian hormone and antral follicle count, while baseline hormonal investigations included follicle-stimulating hormone, luteinizing hormone, thyroid-stimulating hormone, and prolactin.

Ovulation induction was performed according to the treating physician's clinical assessment using agents such as letrozole, clomiphene citrate, or gonadotropins. Follicular development was monitored by serial transvaginal ultrasonography. The number of developing follicles, number of mature follicles, and diameter of the dominant follicle were documented during the treatment cycle. Endometrial thickness was measured in the sagittal plane at the thickest portion of the endometrium, and the endometrial pattern was categorized as trilaminar or non-trilaminar. Serum estradiol was assessed around the day of ovulation triggering where indicated. An hCG trigger was administered when satisfactory follicular maturation was achieved according to the treatment protocol.
Following ovulation, serum progesterone was measured during the mid-luteal phase as an indicator of luteal hormonal response. Information regarding luteal progesterone supplementation was also recorded. Implantation outcome was assessed by serum β-hCG testing at the appropriate post-ovulation interval. Implantation success was defined as a positive biochemical pregnancy test following the monitored induction cycle. Where clinically available, subsequent ultrasonographic evidence of an intrauterine gestational sac was recorded as confirmation of clinical pregnancy; however, the principal study outcome was implantation success versus unsuccessful implantation.
All collected data were entered and analyzed using IBM SPSS Statistics. Continuous variables such as age, BMI, hormonal levels, follicular diameter, and endometrial thickness were summarized as mean ± standard deviation for approximately normally distributed data, while categorical variables were presented as frequencies and percentages. The successful and unsuccessful implantation groups were compared using the independent-samples t-test for continuous variables and the chi-square test or Fisher's exact test for categorical variables, as appropriate. Variables demonstrating clinically relevant or statistically significant associations with implantation success were entered into a multivariable binary logistic regression model. Adjusted odds ratios with 95% confidence intervals were calculated to identify independent predictors of successful implantation. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 89 women was analyzed, who were undergoing ovulation induction. Successful implantation was noted in 36 women (40.4%) while the other 53 women (59.6%) failed. To identify factors which may be associated with the success of implantation, the two groups were compared with respect to their demographic, hormonal, ovarian, endometrial, and treatment-related characteristics.

Table 1. Baseline demographic and infertility characteristics of the study participants

Variable	Total (n=89)	Successful implantation (n=36)	Unsuccessful implantation (n=53)	p-value
Age, years, mean ± SD	30.8 ± 4.6	29.2 ± 3.9	31.9 ± 4.7	**0.006**
BMI, kg/m², mean ± SD	25.7 ± 3.8	24.6 ± 3.2	26.5 ± 4.0	**0.020**
Duration of infertility, years, mean ± SD	4.3 ± 2.2	3.7 ± 1.8	4.8 ± 2.3	**0.018**
Primary infertility, n (%)	57 (64.0)	22 (61.1)	35 (66.0)	0.637
Secondary infertility, n (%)	32 (36.0)	14 (38.9)	18 (34.0)	
Previous fertility treatment, n (%)	31 (34.8)	10 (27.8)	21 (39.6)	0.249

The mean BMI and the mean age were significantly lower for women who implant than women who do not implant. Women who had an implant were also less likely to have had a longer period of infertility. In contrast, there was no significant difference between the two groups in the distribution of primary and secondary infertility.

Table 2. Hormonal profile according to implantation outcome

Hormonal parameter	Successful implantation (n=36)	Unsuccessful implantation (n=53)	p-value
AMH, ng/mL	3.1 ± 1.2	2.4 ± 1.1	**0.005**
Baseline FSH, IU/L	6.8 ± 1.7	7.7 ± 2.0	**0.030**
Baseline LH, IU/L	6.2 ± 2.1	6.6 ± 2.3	0.410
Estradiol on trigger day, pg/mL	238.4 ± 71.6	199.7 ± 68.5	**0.012**
Mid-luteal progesterone, ng/mL	15.8 ± 4.5	11.9 ± 4.2	**<0.001**
Prolactin, ng/mL	14.9 ± 4.1	15.7 ± 4.6	0.401
TSH, mIU/L	2.18 ± 0.76	2.35 ± 0.81	0.323

Successful implantations were associated with significantly higher mean AMH, trigger-day estradiol and mid-luteal progesterone levels in the women. The FSH level in the successful implantation group was significantly lower, in contrast. LH, prolactin and TSH levels were not significantly different.

Table 3. Follicular, endometrial, and physiological characteristics

Parameter	Successful implantation (n=36)	Unsuccessful implantation (n=53)	p-value
Antral follicle count	11.4 ± 3.2	9.7 ± 3.1	**0.014**
Dominant follicle diameter, mm	20.1 ± 1.8	18.8 ± 2.1	**0.003**
Number of mature follicles	2.3 ± 0.9	1.8 ± 0.8	**0.008**
Endometrial thickness, mm	9.8 ± 1.5	8.5 ± 1.6	**<0.001**
Trilaminar endometrium, n (%)	29 (80.6)	30 (56.6)	**0.019**
Systolic BP, mmHg	116.3 ± 9.8	118.6 ± 10.5	0.300
Diastolic BP, mmHg	74.2 ± 7.4	75.8 ± 7.9	0.340
Resting pulse rate, beats/min	78.1 ± 7.6	79.5 ± 8.2	0.421

Higher number of antral follicles, larger dominant follicle diameter, higher number of mature follicles and greater endometrial thickness were associated with successful implantation. Women who did implant had significantly more likely to have a trilaminar endometrial pattern. There was no significant relationship between blood pressure and resting pulse rate and outcome of implantation.

Table 4. Ovulation-induction and treatment-related characteristics

Treatment characteristic	Successful implantation (n=36)	Unsuccessful implantation (n=53)	p-value
Letrozole-based induction, n (%)	21 (58.3)	29 (54.7)	0.738
Clomiphene citrate, n (%)	9 (25.0)	16 (30.2)	0.593
Gonadotropin-based induction, n (%)	6 (16.7)	8 (15.1)	0.842
hCG trigger administered, n (%)	33 (91.7)	43 (81.1)	0.167
Luteal progesterone support, n (%)	30 (83.3)	38 (71.7)	0.207
Stimulation duration, days	10.2 ± 1.8	10.7 ± 2.0	0.231

There were no significant differences between the two groups, whether they were successful or not, in the type of ovulation-induction medication, hCG trigger, luteal progesterone supplementation and/or the length of the ovarian stimulation period.

Table 5. Association of selected clinical predictors with implantation success

Predictor	Implantation success n/N (%)	p-value
Age <35 years	32/67 (47.8)	**0.018**
Age ≥35 years	4/22 (18.2)	
BMI <25 kg/m²	21/40 (52.5)	**0.028**
BMI ≥25 kg/m²	15/49 (30.6)	
Endometrial thickness ≥8 mm	34/70 (48.6)	**0.003**
Endometrial thickness <8 mm	2/19 (10.5)	
Dominant follicle ≥18 mm	34/73 (46.6)	**0.009**
Dominant follicle <18 mm	2/16 (12.5)	
Trilaminar endometrium	29/59 (49.2)	**0.019**
Non-trilaminar endometrium	7/30 (23.3)	

Implantation success was significantly more frequent among women younger than 35 years, those with BMI below 25 kg/m², an endometrial thickness of at least 8 mm, a dominant follicle diameter of at least 18 mm, and a trilaminar endometrial pattern.

Table 6. Multivariable logistic regression analysis of predictors of successful implantation

Predictor	Adjusted OR	95% CI	p-value
Age, per 1-year increase	0.86	0.75–0.98	**0.024**
BMI, per 1-kg/m² increase	0.88	0.77–1.00	0.052

AMH, per 1-ng/mL increase	1.56	1.06–2.31	**0.025**
Estradiol on trigger day	1.01	1.00–1.02	0.071
Mid-luteal progesterone, per 1-ng/mL increase	1.19	1.06–1.34	**0.004**
Dominant follicle diameter, per 1-mm increase	1.31	1.03–1.67	**0.029**
Endometrial thickness, per 1-mm increase	1.62	1.15–2.29	**0.006**
Number of mature follicles	1.29	0.83–2.00	0.257

After adjustment for potential confounding variables, younger age, higher AMH concentration, higher mid-luteal progesterone, greater dominant follicle diameter, and increased endometrial thickness remained significant independent predictors of successful implantation. Among these factors, endometrial thickness and mid-luteal progesterone demonstrated particularly strong associations with implantation outcome.

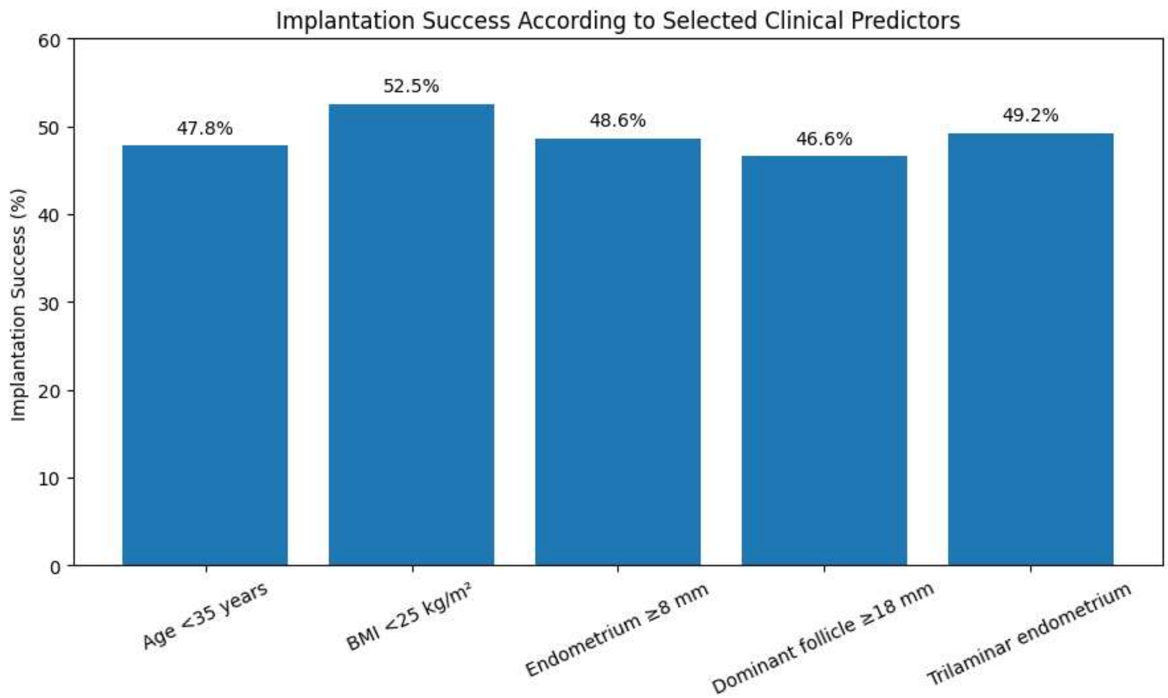

Figure 1. Implantation success according to selected physiological and clinical predictors among women undergoing ovulation induction (n = 89).

DISCUSSION

The present study evaluated physiological, hormonal, follicular, and endometrial factors associated with implantation success among women undergoing ovulation induction. Successful implantation was observed in 36 of 89 women, representing an implantation rate of 40.4%. The findings indicated that implantation was not dependent on a single factor; rather, it appeared to result from the combined influence of maternal age, ovarian reserve, hormonal response, follicular development, and endometrial receptivity. Women who achieved implantation generally had a more favorable reproductive profile than those in whom implantation was unsuccessful (11, 12).

The implantation outcome was related to age. Successful implantation was seen to be lighter than unsuccessful ones; and women below age 35 had a much higher rate of successful implantation. This is biologically reasonable since as women get older, both the number and quality of oocytes decrease over time. Some changes are also associated with the aging of the woman and may cause chromosomal abnormalities in the oocyte and early embryo, and make it less likely for successful implantation to occur. Ovulation induction can improve follicular recruitment and ovulation, but it cannot completely counteract the negative reproductive effects of advanced maternal age. This is reflected in the association found in the present study which confirms that maternal age should be included in clinical evaluation prior to treatment planning (13-15).

Woman who had a successful implantation showed a lower BMI and woman with BMI less than 25 kg/m2 showed a higher implantation rate. Overweight may affect fertility by a number of mechanisms including changes in insulin sensitivity, ovarian steroidogenesis, inflammatory pathways, and endometrial function. These changes can disrupt the normal development of the follicles and the synchrony necessary between the embryo and the endometrium. BMI was not a significant independent predictor in the present multivariable analysis, but association in the initial comparison

indicates that metabolic health could be a factor influencing reproductive outcomes. Pre-treatment counseling on weight management therefore may be useful, especially in the case of women who are overweight or obese (16, 17).
Hormonal results showed that women who had a successful implantation had higher AMH, estradiol, and mid-luteal progesterone levels, and lower baseline FSH levels. AMH is used as a marker of ovarian reserve and represents the number of follicles ready to be recruited. Thus, higher AMH levels are potentially linked to a better response to stimulation. On the other hand, elevated basal FSH may be related to decreased ovarian reserve and a less responsive ovary to induction. On the trigger day, Estradiol will indicate follicular activity and maturation and adequate Progesterone following the ovulation will be necessary for secretory transformation of the endometrium. The high correlation of mid-luteal progesterone and successful implantation found in the present study highlights the significance of proper luteal hormonal support for an endometrium conducive to implantion (18, 19).
The follicular characteristics were also significantly associated with implantation. Women who implanted had larger dominant follicles, increased antral follicle count and increased number of mature follicles. The implantation rate was significantly higher with a dominant follicle greater than or equal to 18 mm compared with smaller follicular measurements. However, the release of a competent oocyte requires appropriate follicular maturation and suboptimal follicular development may have been linked to suboptimal oocyte maturation and/or corpus luteum function. However, there is also a need to avoid excessive follicular recruitment as this may increase the risk of multiple pregnancy. The findings indicate that such monitoring of ultrasound is important during the cycles of ovulation induction (19).
The endometrium seemed to be one of the best physiological components that correlated best with successful implant. The women who were successfully implanted had a higher mean endometrial thickness and more women had a trilaminar endometrial pattern. The response of the uterine lining to ovarian steroid hormones reflects adequate endometrial development which is necessary for the development of the proper environment for the embryo to implant and grow. A trilaminar shape around the peri-ovulatory period is also usually regarded as a good ultrasonographic characteristic. The multivariable model showed that endometrial thickness was an independent risk factor for implantation suggesting that endometrial assessment could also be clinically useful for predicting cycle outcome (8, 20).
In this study, no significant difference was observed in the type of ovulation induction drug used and the likelihood of implantation. Letrozole and clomiphene citrate and gonadotropin based treatment were used in similar number of women in both the successful and unsuccessful group. This implies that when treatment is selected appropriately the biological response to induction may be more important than the specific medication used. Similarly, there were no significant differences in the duration of stimulation, hCG triggering or progesterone supplementation between the groups. The results do not mean these therapeutic factors are not important, but rather may be because of variable treatments selected and the relatively small sample size.
Multivariable logistic regression also showed that age, AMH, mid-luteal P, dominant follicle diameter and endometrial thickness were independent factors for successful implantation. The results confirm the need to adopt a multifactorial strategy for predicting outcomes of fertility treatments. Patient characteristics associated with ovarian reserve markers, hormonal response, follicular maturation and endometrial measurements could prove a more meaningful assessment of ovarian responses than any one of these parameters in routine clinical practice. This information can help physicians counsel patients and tailor treatment courses and may help them find cycles where there is a relatively low likelihood of implantation.

LIMITATIONS OF FINDINGS

This study was done in a single institution with 89 participants, which may not be representative of other groups and fertility-care settings. Other factors that may be involved in the implantation process such as detailed semen parameters, genetic abnormalities, lifestyle factors, insulin resistance, inflammatory biomarkers and embryo-related characteristics were not included in the analysis. Moreover, the primary endpoint for the implantation was biochemical pregnancy and longer-term outcomes like continuing pregnancies and live births were not the primary endpoints. Multicenter studies with larger number of patients and longer follow-up are warranted to assess their potential as prediction models for implantation, clinical pregnancy and live birth by combining hormonal markers with ultrasonographic markers.

CONCLUSION

Implantation success among women undergoing ovulation induction was associated with several interacting physiological and hormonal factors. Younger maternal age, higher AMH concentration, adequate mid-luteal progesterone, larger dominant follicle diameter, and greater endometrial thickness were identified as important independent predictors of successful implantation. A trilaminar endometrial pattern, higher estradiol levels, greater antral follicle count, and a higher number of mature follicles were also associated with favorable implantation outcomes.

These findings indicate that successful implantation depends on the coordinated response of the ovary and endometrium rather than on the ovulation-induction medication alone. Assessment of ovarian reserve, follicular maturation, luteal hormonal status, and endometrial receptivity may therefore help clinicians estimate the probability of implantation and individualize treatment strategies. Larger prospective studies are recommended to confirm these predictors and determine their usefulness in forecasting clinical pregnancy and live-birth outcomes.

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