BIOMEDICINSKA ISTRAŽIVANJA
2025;16(2):1–8

UDK: 618.177-089.888.11
DOI: 10.59137/BII202502532T

Original article

Association of parameters of ovarian hormonal hyperstimulation with assisted reproductive technology outcomes in infertile women

Daniela Telebak[1], Djordje Čekrlija[2], Milena Todorović[1], Slobodan Stanić[1], Dalibor Mihajlović[3]

[1]College of Health Sciences Doboj, Nursing Study Program, Doboj, Republic of Srpska, Bosnia and Herzegovina

[2]University of Banja Luka, Faculty of Philosophy, Department of Psychology, Banja Luka, Republic of Srpska, Bosnia and Herzegovina

[3]University of Banja Luka, Faculty of Medicine, Department of Emergency Medicine, Banja Luka, Republic of Srpska, Bosnia and Herzegovina

Primljen – Received: 16/09/2025
Prihvaćen – Accepted: 26/11/2025

Corresponding author:
Daniela Telebak, MD, PhD
Vojvode Sindjelića 45, 74 000 Doboj
e-mail: daniela.telebak@gmail.com

Copyright: ©2025 Daniela Telebak et al. This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 International (CC BY 4.0) license.

Summary

Introduction. This study analyzed the factors influencing the outcome of assisted reproductive technology (ART) in women with infertility issues. The investigation focused on endometrial thickness, the number of retrieved oocytes, and the number of obtained embryos as potential predictors of ART success.

Method. A health-epidemiological questionnaire of general data was created for the purposes of this study. Various statistical methods were applied for data analysis. Descriptive statistical parameters for the observed parameters were presented, including the arithmetic mean (M), standard deviation (SD), skewness (Sk), and kurtosis (Ku), to examine deviations from the normal distribution. Multiple regression analysis was applied to investigate the relationships of the independent variables with the dependent variable.

Results. The study included 100 women of reproductive age. Endometrial thickness was not a significant predictor of ART outcome. Conversely, the number of retrieved oocytes and the number of obtained embryos were identified as significant predictors of ART success. Participants with positive ART outcomes demonstrated a lower number of retrieved oocytes but a higher number of obtained embryos.

Conclusion. These findings highlight the importance of embryo quality in the implantation process. Further research is needed to better understand this dynamic and to improve infertility treatments.

Key words: assisted reproductive technology, infertility, endometrial thickness, number of retrieved oocytes

Introduction

The synchronization between embryonic development and endometrial receptivity constitutes a fundamental determinant of successful medically assisted reproduction [1]. During this process, the endometrium undergoes complex biochemical and morphological changes,

thereby establishing an optimal microenvironment for potential embryo implantation. This critical interval is commonly referred to as the window of implantation.

Since the introduction of controlled ovarian hyperstimulation protocols in assisted reproductive technologies, continuous refinements have been undertaken to prevent premature luteinization and to enhance treatment outcomes. Nevertheless, despite these advances, the overall success rate of assisted reproductive procedures remains limited, with live birth rates estimated at approximately 25%.

In the majority of cases, implantation failure in infertile women results from inadequate endometrial receptivity. Only in approximately one-third of these cases implantation failure is attributable to poor embryo quality. Interestingly, despite these observations, controlled ovarian hyperstimulation has predominantly been directed toward improving oocyte and embryo quality, while the potential detrimental impact of high hormonal doses on the endometrium is often overlooked.

Controlled ovarian hyperstimulation represents a pivotal component of assisted reproductive procedures, shifting clinical practice from natural monofollicular cycles to multifollicular stimulated cycles. Within this process, the ovarian response to hormonal stimulation emerges as a critical determinant and is influenced by both age and ovarian reserve. Although numerous studies have been published addressing the number of retrieved oocytes and the outcomes of assisted reproduction, the results remain frequently inconsistent and controversial [2–7].

Some researchers suggest that a higher number of retrieved oocytes may increase the likelihood of successful conception [3, 4], while others propose that mild ovarian stimulation with fewer retrieved oocytes could optimize implantation rates [6]. Nevertheless, paradoxical situations are frequently encountered, in which a large number of oocytes obtained during controlled ovarian hyperstimulation may result in lower fertilization rates due to an increased proportion of immature oocytes. This paradox may be explained by previous research indicating cytoplasmic immaturity of oocytes [8].

In natural reproductive processes, oocyte maturation is the outcome of a finely tuned and time-dependent selection. However, standard controlled ovarian hyperstimulation protocols may override this natural selection, leading to the maturation of oocytes with compromised quality. Such oocytes can significantly contribute to the failure of assisted reproductive procedures, as they may interfere with embryo development and induce other adverse effects [9]. The quality of oocytes is determined not only by the nuclear and mitochondrial genome but also by the ovarian microenvironment and the preovulatory follicle, both of which may substantially influence transcriptional and translational processes. Within this complex framework, it is unlikely that any single factor or characteristic can adequately predict the developmental competence of oocytes.

Oocyte maturity plays a pivotal role in achieving successful fertilization, embryo development, and pregnancy. Attaining adequate oocyte maturity and the biosynthesis of appropriate estradiol levels requires precise actions of luteinizing and follicle-stimulating hormones on the theca and granulosa cells. By improving oocyte utilization, the need for stimulation aimed at retrieving larger numbers of oocytes may be reduced. However, the challenge lies in determining the optimal gonadotropin dosage and in the efficient use of retrieved oocytes, given that not every oocyte is capable of developing into a high-quality embryo.

The objective of this study was to investigate potential factors influencing the outcomes of assisted reproductive technology (ART) in women of reproductive age with infertility. Specifically, the study examined the relationship between endometrial thickness, the number of retrieved oocytes, and embryos with ART outcomes. Furthermore, it analyzed how these factors interact in determining the success of

ART. Understanding these associations has the potential to improve the management of infertility treatments and enhance pregnancy rates in patients undergoing ART procedures.

Methods

Sample Description

This prospective cohort study included a convenience sample of 100 women of reproductive age with infertility. The participants' ages ranged from 23 to 40 years, with a mean age of 32.09 years (standard deviation [SD] = 4.18). Of the total sample, 86 women were married, while 14 were living in a common-law partnership. Regarding educational attainment, one participant had completed primary school, three vocational school, 50 secondary school, and 44 had higher education or a university degree. In terms of employment, 73 participants were employed, while 27 were unemployed. Concerning blood groups, 43 participants had blood group A, 11 AB, 18 B, and 28 O.

Data Collection

Data were collected at the Clinic for Gynecology, Infertility Treatment, and In Vitro Fertilization Medico-S in Banja Luka. The study was conducted with prior approval from the Ethics Committee, and all participants provided written informed consent after being fully informed about the purpose and procedures of the study. Participants were also assured of the confidential and voluntary nature of their involvement.

Questionnaire and variables

For the purposes of this study, a health-epidemiological questionnaire was designed to collect general demographic and medical information, including age, marital status, education level, employment status, past medical history, tobacco use, physical activity, and other relevant data.

Stimulation protocol

All participants underwent stimulation with a short protocol, whereby gonadotropin administration began on day 2 of the menstrual cycle, and a GnRH antagonist was introduced between days 6 and 9.

Parameter measurement

During the study, several parameters related to the outcome of ovarian hormonal stimulation were measured, including endometrial thickness, follicular growth, the number of retrieved oocytes, the number of mature oocytes, and the number of embryos obtained.

Statistical analysis

Data were analyzed using descriptive and inferential statistical methods. Descriptive statistics included the calculation of mean (M), standard deviation (SD), skewness (Sk), and kurtosis (K) to assess normality of data distribution. Skewness values close to zero indicated symmetry, while positive kurtosis values suggested elongated (leptokurtic) distributions.

To examine associations between continuous and categorical variables, several statistical tests were applied:

- Simple linear regression was used to test the hypothesis that greater endometrial thickness might be associated with a higher likelihood of a positive ART outcome,
- Independent samples t-test was conducted to compare endometrial thickness between women who achieved pregnancy and those who did not,

- Point-biserial correlation analysis assessed the relationship between ART outcome (binary variable) and quantitative parameters — number of retrieved oocytes, mature oocytes, and embryos,
- Multiple linear regression analysis was performed to determine whether the number of retrieved oocytes, mature oocytes, and embryos could jointly predict ART outcomes.

A p-value < 0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics software (IBM Corp., Armonk, NY, USA).

Results

Descriptive Analysis and Endometrial Thickness

Descriptive statistics for the measured parameters - endometrial thickness, number of retrieved oocytes, number of mature oocytes, and number of embryos - are detailed in Table 1. Endometrial thickness ranged from 5.60 to 17.00 mm, with a mean value of 10.55 mm 1.96 mm. The mean number of retrieved oocytes was 9.72 mm 5.89.

The independent samples t-test (Table 2) comparing endometrial thickness between groups revealed no statistically significant difference in endometrial thickness between participants who achieved pregnancy (Positive outcome: M = 10.79 mm 2.16 mm) and those who did not (Negative outcome: M = 10.51 mm 1.87 mm; t = -0.69, df = 98, p = 0.492). Consequently, endometrial thickness was not a significant prognostic factor for ART success in this study.

Table 2. T-test of endometrial thickness by ART outcome

Outcome	M	SD	t	df	p
Negative	10.51	1.87	-0.69	98	0.492
Positive	10.79	2.16			

Predictive Analysis of Oocyte and Embryo Parameters

Point-biserial correlation analysis (Table 3) showed that, individually, none of the quantitative parameters were significantly correlated with the binary ART outcome (p > 0.05).

A multiple linear regression model was performed to determine the joint predictive power of the number of retrieved oocytes, mature oocytes, and embryos on ART outcome. The results (Table 4) indicate that these three variables collectively constituted a statistically significant set of predictors of ART outcome (R = 0.285; F(3, 95) = 2.840; p = 0.042), explaining 8.2\ % of the total variance (R^2 = 0.082).

Examination of the individual regression coefficients (Table 5) confirmed that the number of retrieved oocytes (beta = -0.333, p = 0.027) and the number of embryos (beta = 0.387, p = 0.026) were statistically significant predictors. This finding suggests that participants with a positive ART outcome tended to have a lower number of retrieved oocytes but a higher number of obtained embryos. The number of

Table 1. Descriptive statistics of endometrial thickness, number of retrieved oocytes, and number of embryos

Parameter	Minimum	Maximum	M	SD	Sk	K
Endometrial thickness (mm)	5.60	17.00	10.55	1.96	-0.04	1.78
Number of retrieved oocytes	1.0	35.0	9.72	5.89	1.51	3.53
Number of mature oocytes	0.0	25.0	7.59	4.46	1.19	2.51
Number of embryos	1.0	19.0	5.47	3.33	1.35	2.22

Table 3. Point-biserial correlations between ART outcome and number of retrieved oocytes, mature oocytes, and embryos

Variable	ART outcome	Retrieved oocytes	Mature oocytes	Embryos
Retrieved oocytes	-.119	1		
Mature oocytes	-.002	.742**	1	
Embryos	.096	.674**	.811**	1

**correlation significant at $p < 0.01$

mature oocytes was not a significant predictor in the final regression model (beta = -0.083, p = 0.659).

Table 4. Multiple regression parameters

R	R^2	F	df1	df2	p
0.285	0.082	2.840	3	95	0.042

Table 5. Regression coefficients

Predictor	β	p
Retrieved oocytes	-0.333	0.027
Mature oocytes	-0.083	0.659
Embryos	0.387	0.026

These analyses and results demonstrate a significant relationship between the number of retrieved oocytes and embryos with ART outcome, whereas no association was observed between endometrial thickness or the number of mature oocytes and ART outcome.

Discussion

The primary objective of this study was to evaluate the predictive capacity of endometrial thickness, retrieved oocyte count, and embryo count on ART outcomes. Our findings offer important clinical insights into the relative influence of these parameters on implantation success.

Endometrial Thickness and Receptivity

In alignment with previous work [12, 13], our study found no statistically significant correlation between endometrial thickness and the likelihood of a positive ART outcome (Table 2). Although endometrial thickness is routinely used as an indicator of uterine receptivity, our results support the growing body of literature [6, 7] suggesting that receptivity is a far more complex, multi-dimensional trait influenced by various hormonal and biochemical factors [10, 11] rather than a single morphological measurement. This finding challenges the general assumption that greater endometrial thickness necessarily ensures a higher pregnancy rate, despite some studies reporting such an association [14–17].

Ovarian Response and Embryo Quality

In contrast, the multiple regression analysis identified the number of retrieved oocytes and the number of obtained embryos as statistically significant predictors of ART success (Table 5). The findings presented a particularly complex relationship: success was associated with a lower number of retrieved oocytes, but a higher number of resulting embryos.

The negative correlation with the number of retrieved oocytes (beta = -0.333) supports the hypothesis that very intensive controlled ovarian hyperstimulation may compromise

oocyte quality [20], potentially leading to a higher proportion of immature oocytes [8] or aneuploidy [15]. This is consistent with studies advocating for milder ovarian stimulation protocols to optimize implantation rates [6, 14].

Conversely, the strong positive association with the number of obtained embryos (beta = 0.387) decisively highlights the pivotal role of embryo quality, developmental competence, and selection in achieving implantation. The high yield of embryos relative to retrieved oocytes suggests that effective selection criteria or inherently better oocyte quality among this successful group mitigated the need for high oocyte numbers. These dynamics underscore that the transition from retrieved oocyte to viable embryo is the critical checkpoint in the ART process.

Limitations and Future Directions

A limitation of this study is the relatively low percentage of variance explained by the model (R^2 = 0.082), suggesting that other unmeasured factors (e.g., specific molecular markers of endometrial receptivity, sperm quality, or genetic factors) significantly contribute to ART outcomes. Further research should focus on clarifying the optimal balance between ovarian stimulation intensity and oocyte developmental competence to personalize treatment protocols.

Conclusion

This study examined factors influencing assisted reproductive technology (ART) outcomes in infertile women of reproductive age. Among the analyzed parameters, the number of retrieved oocytes and embryos were identified as significant predictors of ART success, while endometrial thickness showed no statistically significant impact. These results highlight that embryo quality is more critical than the number of oocytes retrieved.

Further studies are needed to clarify the complex interactions among ovarian response, patient characteristics, and implantation potential, aiming to optimize individualized infertility treatments and to improve ART success rates. The authors thank all participants and the Clinic for Gynecology, Infertility Treatment, and In Vitro Fertilization Medico-S in Banja Luka for their valuable support.

Funding source. The authors received no specific funding for this work.

Ethical approval. The Ethics Committee of the Clinic for Gynecology, Infertility Treatment, and In Vitro Fertilization Medico-S, Banja Luka, Republic of Srpska, Bosnia and Herzegovina, approved the study and informed consent was obtained from all individual respondents. The research was conducted according to the Declaration of Helsinki.

Conflicts of interest. The authors declare no conflict of interest.

References:

1. Tabibzadeh S. Molecular control of the implantation window. Human Reprod Update 1998;4(5):465–71.
2. Check JH, Dietterich C, Graziano V, Lurie D, Choe JK. Effect of maximal endometrial thickness on outcome after frozen embryo transfer. Fertil Steril 2004;81(5):1399–400.
3. Groenewoud ER, Cohlen BJ, Al-Oraiby A, Brinkhuis EA, Broekmans FJM, de Bruin JP, et al. Influence of endometrial thickness on pregnancy rates in modified natural cycle frozen-thawed embryo transfer. Acta Obstet Gynecol Scand 2018;97(7):808–15.
4. Shaodi Z, Qiuyuan L, Yisha Y, Cuilian Z. The effect of endometrial thickness on pregnancy outcomes of frozen-thawed embryo transfer cycles which underwent hormone replacement therapy. PLoS ONE 2020;15(9):e0239120.
5. Kasius A, Smit JG, Torrance HL, Eijkemans MJC, Mol BW, Opmeer BC, et al. Endometrial thickness and pregnancy rates after IVF: a systematic review and meta-analysis. Hum Reprod Update 2014;20(4):530–41.
6. Momeni M, Kovanci E, Rahbar M. A meta-analysis of the relationship between endometrial thickness and outcome of in vitro fertilization cycles. J Hum Reprod Sci 2011;4(3):130–7.
7. Yurci A, Dokuzeylul Gungor N, Gurbuz T. High Endometrial Thickness Does not Affect IVF/ICSI Outcomes. Eur J Ther 2021;27(1):94–8.
8. Kovacs P, Matyas S, Boda K, Kaali SG. The effect of endometrial thickness on IVF/ICSI outcome. Hum Reprod 2003;18(11):2337–41.
9. Al-Ghamdi A, Coskun S, Al-Hassan S, Al-Rejjal R, Awartani K. The correlation between endometrial thickness and outcome of in vitro fertilization and embryo transfer (IVF-ET) outcome. Reprod Biol Endocrinol 2008;6:37.
10. Wu Y, Gao X, Lu X, Xi J, Jiang S, Sun Y, et al. Endometrial thickness affects the outcome of in vitro fertilization and embryo transfer in normal responders after GnRH antagonist administration. Reprod Biol Endocrinol 2014;12:96.
11. Rombauts L, McMaster R, Motteram C, Fernando S. Risk of ectopic pregnancy is linked to endometrial thickness in a retrospective cohort study of 8120 assisted reproduction technology cycles. Hum Reprod 2015;30(12):2846–52.
12. Gupta AKR, Gupta RKR. Quantitative and morphological analysis of endothelial cells of donor corneas. Kerala J Ophthalmol 2018;30(2):103–6.
13. Veleva Z, Järvelä IY, Nuojua-Huttunen S, Martikainen H, Tapanainen JS. An initial low response predicts poor outcome in in vitro fertilization/intracytoplasmic sperm injection despite improved ovarian response in consecutive cycles. Fertility and Sterility 2005;83(5):1384–90.
14. Verberg MFG, Eijkemans MJC, Macklon NS, Heijnen EMEW, Baart EB, Hohmann FP, et al. The clinical significance of the retrieval of a low number of oocytes following mild ovarian stimulation for IVF: a meta-analysis. Hum Reprod Update 2009;15(1):5–12.
15. Baart EB, Martini E, Eijkemans MJ, Van Opstal D, Beckers NGM, Verhoeff A, et al. Milder ovarian stimulation for in-vitro fertilization reduces aneuploidy in the human preimplantation embryo: a randomized controlled trial. Hum Reprod 2007;22(4):980–8.
16. Ji J, Liu Y, Tong XH, Luo L, Ma J, Chen Z. The optimum number of oocytes in IVF treatment: an analysis of 2455 cycles in China. Hum Reprod 2013;28(10):2728–34.
17. Hohmann FP, Macklon NS, Fauser BCJM. A Randomized Comparison of Two Ovarian Stimulation Protocols with Gonadotropin-Releasing Hormone (GnRH) Antagonist Cotreatment for in Vitro Fertilization Commencing Recombinant Follicle-Stimulating Hormone on Cycle Day 2 or 5 with the Standard Long GnRH Agonist Protocol. J Clin Endocrinol Metab 2003;88(1):166–73.
18. Kuehn BM. Estimate of New Chronic HCV Cases Lower Than Expected. JAMA 2014;311(12):1188–9.
19. Yoldemir T, Fraser IS. The effect of retrieved oocyte count on pregnancy outcomes in an assisted reproduction program. Arch Gynecol Obstet 2010;281(3):551–6.
20. Swain JE, Pool TB. ART failure: oocyte contributions to unsuccessful fertilization. Hum Reprod Update 2008;14(5):431–46.

Povezanost parametara hormonske hiperstimulacije jajnika sa ishodima asistirane reproduktivne tehnologije kod neplodnih žena

Daniela Telebak[1], Đorđe Čekrlija[2], Milena Todorović[1], Slobodan Stanić[1], Dalibor Mihajlović[3]

[1]Visoka medicinska škola zdravstva Doboj, Studijski program Zdravstvena njega, Doboj, Republika Srpska, Bosna i Hercegovina

[2]Univerzitet u Banjoj Luci, Filozofski fakultet, Katedra za psihologiju, Banja Luka, Republika Srpska, Bosna i Hercegovina

[3]Univerzitet u Banjoj Luci, Medicinski fakultet, Katedra za urgentnu medicinu, Banja Luka, Republika Srpska, Bosna i Hercegovina

Uvod. Ova studija analizirala je faktore koji utiču na ishod biomedicinski potpomognute oplodnje (BPO) kod žena sa problemom infertiliteta. Istraživanje se fokusiralo na debljinu endometrijuma, broj dobijenih jajnih ćelija i broj dobijenih embriona kao potencijalne prediktore uspjeha BPO.

Metod. Za potrebe ove studije kreiran je zdravstveno-epidemiološki upitnik opštih podataka. Za analizu podataka primijenjene su različite statističke metode. Prikazani su deskriptivni statistički parametri za posmatrane varijable, uključujući aritmetičku sredinu (M), standardnu devijaciju (SD), asimetričnost (Sk) i spljoštenost (Ku) radi ispitivanja odstupanja od normalne distribucije. Primijenjena je multipla regresiona analiza radi ispitivanja odnosa nezavisnih varijabli sa zavisnom varijablom.

Rezultati. Studija je obuhvatila 100 žena reproduktivne dobi. Debljina endometrijuma nije bila značajan prediktor ishoda BPO. Nasuprot tome, broj dobijenih jajnih ćelija i broj dobijenih embriona identifikovani su kao značajni prediktori uspjeha BPO. Učesnice sa pozitivnim ishodom BPO pokazale su manji broj dobijenih jajnih ćelija, ali veći broj dobijenih embriona.

Zaključak. Ovi nalazi naglašavaju važnost kvaliteta embriona u procesu implantacije. Potrebna su dalja istraživanja kako bi se ova dinamika bolje razumjela i unaprijedili tretmani neplodnosti.

Ključne riječi: biomedicinski potpomognuta oplodnja, infertilitet, debljina endometrijuma, broj dobijenih jajnih ćelija