Original Article

# Value of Endometrial Echopattern at HCG Administration Day in Predicting IVF Outcome

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**Abstract**

**Background:** Assisted reproductive treatment (ART) cycle is an expensive procedure with low implantation and pregnancy rate; therefore, it is necessary to evaluate the predictors of success in these patients.

**Objective:** The relationship between endometrial echopattern and pregnancy rate was evaluated.

**Methods**: The endometrial echopattern was analyzed prospectively on the day of human chorionic gonadotropin (HCG) administration in 280 *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) cycles with 8–14 mm endometrial thickness at Royan institute in 2013–2014. Based on echopattern, three groups were developed: pattern A (Triple line), pattern B (Heterogeneous-echogen) and pattern C (Homogeneous-echogen). Pregnancy rate (PR) was compared between all groups. Data was analyzed using SPSS (v.18, Chicago, IL, USA), and descriptive tests such as Chi-square and analytical tests like logistic regression, for controlling confounder variables like age.

**Results:** Among 280 patients finally evaluable, the distribution of endometrial echopattern on the day of HCG administration was 127 patients (45.4%) in group A, 98 patients (35%) in group B and 55 patients (19.6%) in group C. The highest PR per transfer pertained to group A (49.6%), and the lowest to group B (32.7%).

**Conclusion:** The presence of pattern A (Triple line) appears more likely to favor pregnancy. Therefore, ultrasonographic evaluation of endometrial echopattern on the day of HCG administration has prognostic value in clinical settings for predicting implantation in ART cycle.

**Keywords:** Assisted reproductive treatment (ART), endometrial echopattern, human chorionic gonadotropin (HCG), *in vitro* fertilization (IVF), transvaginal ultrasound (TVUS)

**Cite this article as:** Ahmadi F, Akhbari F, Zamani M, Ramezanali F, Cheraghi R. Value of Endometrial Echopattern at HCG Administration Day in Predicting IVF Outcome. *Arch Iran Med*. 2017; **20(2):** 101 – 104.

## Introduction

Although there are advanced methods of assisted fertilization, the implantation rate of embryos with appropriate quality remains low during *in vitro* fertilization/embryo transfer (IVF/ET) treatment.

Several factors are associated with successful implantation, including receptivity of endometrium. Nowadays, transvaginal ultrasound (TVUS) with its high-frequency and high resolution capability is used as an improved non-invasive method for assessing endometrial receptivity during assisted reproductive treatment (ART) cycles by new machine. Ultrasound parameters including endometrial thickness, endometrial volume and Doppler study of uterine arteries and endometrial blood flow have been used to assess endometrial receptivity during IVF treatment. The relationship between endometrial echopattern and pregnancy outcome has been published in various articles. The findings of some studies have suggested that pregnancy outcome is better in triple line pattern,[1,3–7] while others have found no relationship between pattern of endometrium and pregnancy outcome.[8–10]

The present prospective study was undertaken to determine whether endometrial pattern on the day of human chorionic gonadotropin (HCG) administration, was related to pregnancy outcome in ART cycles.

## Materials and Methods

This is cross-sectional study conducted between February 2013 and February 2014 at Royan institute, Tehran, Iran on 280 patients undergoing IVF and ICSI cycles. The inclusion criteria included women in first IVF cycle <40 years of age, absence of uterine pathologies (such as polyp, mullerian anomalies, endometrial hyperplasia and fibroma with compressor effect) and absence of any history of uterine surgery. Sagittal thickness of endometrium should be 8–14 mm and at least one of the embryos should be grade A. Any patient with a history of abortion, dilatation and curettage (D&C), treatment hysteroscopy, polypectomy, myomectomy, septum resection or presence of uterine anomalies was excluded

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**Accepted for publication:** 21 December 2016

**Table 1.** Pregnancy and echo pattern cross tabulation.

| | | Pregnancy | | *P*-Value |
|---|---|---|---|---|
| | | Positive | Negative | |
| Echo pattern | Triple line (A) | 63(49.6%) | 64(50.4%) | 0.04 |
| | Heterogeneous-echogen (B) | 32(32.7%) | 66(67.3%) | |
| | Homogeneous-echogen (C) | 20(36.4%) | 35(63.6%) | |
| **Total** | | **115(100%)** | **165(100%)** | |
| **Value are given as *n* (%)** | | | | |

**Table 2.** Effectiveness of confounder variable of study on pregnancy outcome (Logistic Regression).

| | | *P* | OR(95% CI) |
|---|---|---|---|
| Age | | 0.218 | 1.076 |
| BMI | | 0.018 | 1.214 |
| Echo pattern (B) | Reference | | 1 |
| Echo pattern (A) | | 0.01 | 0.50(0.29–0.88) |
| Echo pattern (C) | | 0.54 | 0.80(0.39–1.62) |

from the study. Causes of infertility were PCOs (polycystic ovarian syndrome), unexplained, male factor and tubal factors.

The conventional long protocol with gonadotropin-releasing hormone agonist (GnRHa) was used for ovarian stimulation in all cycles. All patients received OCP-LD (oral contraceptive pill-low dose) from the fifth day of their cycle, then 500 µg/d intracutaneously on the twenty-first day of cycle, dose of the GnRHa were decreased to 200 µgr/d after 12–14 days after GnRH injection and then stimulation was started with daily FSH of 150 IU/ML. Depending on the patient's condition, the dose may decrease or increase. All patients underwent serial ultrasound examination to assess follicular growth until at least 3 follicles with a mean diameter >17mm were seen. On the day of HCG administration, TVUS was performed by an experienced radiologist (at least 13 years of performing sonography) using an Aloka α-10 with a transvaginal 6–7.5 MHz probe (Japan).

Firstly, sagittal thickness was measured in millimeters by placing electronic calipers on the outer walls of the endometrium on the longitudinal axis of the uterine body; if it was between 8 to 14mm, the patient would be included in the study. Endometrial pattern was determined by comparing the reflectivity or gray-scale appearance of the endometrium to that of the adjacent myometrium. It was classified into three types:

A (triple line): A multilayered endometrium consisting of prominent outer and central hyperechogenic lines and inner hypoechogenic or black regions.

B (heterogeneous-echogen): mixed hyperecho and hypoechopattern of endometrium.

C (homogeneous-echogen): increased reflectivity compared to the myometrium and consequently appearing brighter in its gray-scale appearance. The central echogenic line was not visualized. The pregnancy outcome was considered positive, when beta hCG was positive 2 weeks after embryo transferring (ET); thereafter, all patients were followed up by fetal heart detection on sonography. Ethical approval was granted by the ethics committee of the Royan institute. Informed written consent was obtained from all women.

Data was analyzed using SPSS (v.18, Chicago, IL, USA), and descriptive tests such as Chi-square and analytical tests like logistic regression, for controlling confounder variables like age. Data with probability value <0.05 were regarded as significant.

## Results

This is a cross-sectional study from February 2013 to February 2014 in Royan Institute (Tehran, Iran) on patients who underwent IVF/ICSI treatment. This study is a census and all patients who underwent this treatment between 2013 to 2014 were included in study. The mean age of patients was 29.53 ± 4.15 years (range: 20–40) and range of infertility duration was 1–18 years. The percentage of positive pregnancy was 41.1% (n: 115), and 58.9% (n: 165) had negative pregnancy. Among all of the 280 women, on the day of HCG administration, 127 (45.4%) patients exhibited pattern A, 98 (35%) patients exhibited pattern B and 55 (19.6%) patients exhibited pattern C. ICSI , IVF, and ICSI/IVF treatment were 78.1 %, 1.8%, and 20.1%, respectively. Causes of infertility were PCO (7.9%), Tubal factor (8.3%), Unexplained (12.9%), Male factor (68%), and Male-PCO (2.9%). The average level of FSH hormone was 6.46 (±2.48) and the average level of LH hormone was 5.39 (±4.29). BMI was 24.48 (±3.38); in patients who were pregnant, the average BMI was 24.61(±3.52) and in patients who were not pregnant, it was 25.0 (±3.28). There was a statistically significant relationship between pregnancy outcome and endometrial echopattern (Table 1) ($P < 0.05$).

The relationship between endometrial echopattern and pregnancy rate is presented in Table 1. Logistic regression was used to assess effectiveness of some variables in this study on pregnancy outcome (Table 2).

As presented in Table 2, according to multiple logistic regression, there was a statistically significant relationship between BMI and pregnancy rate ($P < 0.05$).

## Discussion

Endometrial receptivity is crucial to implantation of an embryo. Measuring endometrial echopattern during IVF cycle is used routinely to evaluate receptivity. It is determined by relative echogenicity of the endometrium and nearby myometrium that is observed on a longitudinal uterine ultrasonic section.

In the early proliferative phase, the endometrium is homogeneous; by the late proliferative phase, it has the triple line pattern, which probably arises from the central opposing surfaces

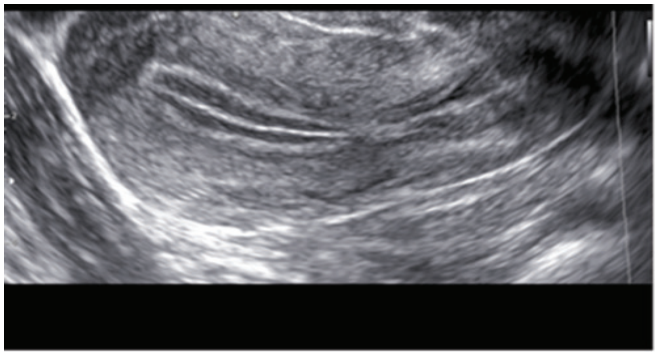

**Figure 1.**Tripple line (A).

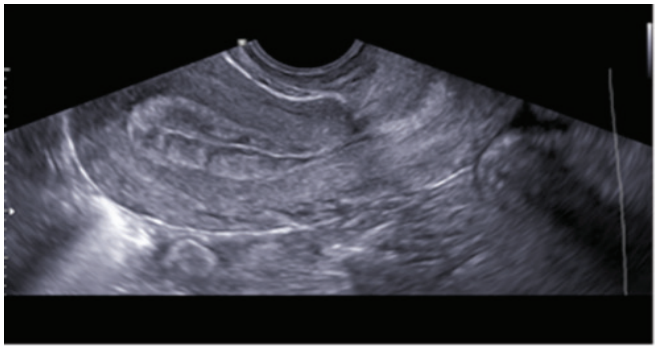

**Figure 2.** Heterogeneous-echogen (B).

**Figure 3.** Homogeneous-echogen pattern (C).

of the endometrium and the outer echogenic basalis layers of the endometrium. No consensus has been reached with regard to the appropriate endometrial echopattern required for successful pregnancy.

The classification of patterns varies from one study to another. In our study, three sonographic endometrial patterns [A (Triple line) (Figure 1), B (Heterogeneous-echogen) (Figure 2) and C (Homogeneous-echogen) (Figure 3)] were defined on the day of HCG administration. The presence of pattern A endometrium on the day of HCG administration was associated with higher pregnancy rate per embryo transfer (ET) in IVF program and pattern B has a lower positive pregnancy rate per ET.

The present result shows the significant difference between endometrial pattern in terms of pregnancy rate and is in agreement with other studies results,[1,4,6,7,11–18,22] which have also reported higher pregnancy rates in women with endometrium displaying triple line (pattern A) on the day of HCG administration, while others indicated no difference in endometrial pattern between patients who became pregnant and those who did not.[8–10,12,15]

In some other previous studies, the results have been different. Check *et a1*. and Serafini *et al.* confirmed the negative influence of homogeneous hyperechoic endometrial echopattern on PRs following the luteal phase Leuprolide acetate-HMG ovarian stimulation regimen.[13,16] Bohrer *et al.* demonstrated that in patients receiving menotropins, a homogeneous pattern constitutes a bad prognostic sign for pregnancy regardless of endometrial thickness. However, Alborzi *et al*. reported that in patients with a trilaminar pattern, pregnancy rate was equal to those who had a homogenous pattern.[21] Sharara *et al.* (1999) concluded that triple line pattern on the day of oocyte retrieval has a predictive value for pregnancy outcome.[22]

Fleischer *et al.* (1991) reported that multilayered endometrium (the same as pattern A in this study) on the day of HCG administration was associated with a statistically higher chance of conception,[4] which is similar to our findings. On the other hand, in contrast to our results, Ueno *et al.* (1991) reported that mix pattern (outer hyperechogenic and inner hypoechogenic layer), classified as pattern B in this study, had a greater proportion of pregnancy compared to other echo patterns in that study.[14] Also, Hock *et al.* showed that homogeneous endometrial pattern on the day of HCG administration predicts a significantly decreased PR compared with a triple line pattern.[18]

In contrast to our results, some studies in the literature have stated that endometrial pattern is not a significant indicator for predicting pregnancy.[23–25]

According to some studies,[15,19,20] embryo quality is one of the confounding factors in successful implantation rate; in order to prevent this bias, one of the inclusion criteria in our study was good quality of embryo in embryo transferring (most of them were grade A or B). In order to make definitive conclusions, further studies are needed with combined analysis of endometrial sonographic appearance and embryo quality is needed.

The conclusion from these data is that endometrial ultrasound echopattern may be valuable for predicting pregnancy rate and ART cycles on the day of HCG administration. We believe that the findings of the present study will be helpful for decision-making in ART cycles; with an unfavorable endometrial pattern, oocyte cryopreservation is sometimes necessary for successful ART cycle treatment. If pattern is not suitable on the day of HCG administration, careful consideration should be given to oocyte recovery and transfer of frozen embryos during subsequent cycles when more favorable endometrium is detected.

## Acknowledgment

*The authors wish to thank imaging department staff for their*

*assistance in figure preparation.*

## References


1. Welker BG, Gembruch U, Diedrich K, al-Hasani S, Krebs D. Transvaginal sonography of the endometrium during ovum pickup in stimulated cycles for in vitro fertilization. J Ultrasound Med. 1989; 8(10): 549 – 553.
2. Narendra Malhotra JM. Transvaginal sonography in infertility. In: Rao KA, ed. *The Infertility Manual*. 3rd ed. New Dehli: Jitendar P Vij; 2009: 28 – 54.
3. Smith B, Porter R, Ahuja K, Craft I. Ultrasonic assessment of endometrial changes in stimulated cycles in an *in vitro* fertilization and embryo transfer program. J In Vitro Fert Embryo Transf. 1984; 1(4): 233 – 288.
4. Fleischer AC, Herbert CM, Hill GA, Kepple DM, Worrell JA. Transvaginal sonography of the endometrium during induced cycles. J Ultrasound Med. 1991; 10(2): 93 – 95.
5. Check JH, Dietterich C, Lurie D. Non-homogeneous hyperechogenic pattern 3 days after embryo transfer is associated with lower pregnancy rates. Hum Reprod. 2000; 15(5): 1069 – 1074.
6. Sher G, Herbert C, Maassarani G, Jacobs MH. Assessment of the late proliferative phase endometrium by ultrasonography in patients undergoing *in-vitro* fertilization and embryo transfer (IVF/ET). Hum Reprod. 1991; 6(2): 232 – 237.
7. Coulam CB, Bustillo M, Soenksen DM, Britten S. Ultrasonographic predictors of implantation after assisted reproduction. Fertil Steril. 1994; 62(5): 1004 – 1010.
8. khalifa E, Brzyski RG, Oehninger S, Acosta AA, Muasher SJ. Sonographic appearance of the endometrium: the predictive value for the outcome of *in-vitro* fertilization in stimulated cycles. Hum Reprod. 1992; 7(5): 677 – 680.
9. Eichler C, Krampl E, Reichel V, Zegermacher G, Obruca A, Strohmer H, et al. The relevance of endometrial thickness and echo patterns for the success of *in vitro* fertilization evaluated in 148 patients. J Assist Reprod Genet. 1993; 10(3): 223 – 227.
10. Oliveira JB, Baruffi RL, Mauri AL, Petersen CG, Borges MC, Franco JG Jr. Endometrial ultrasonography as a predictor of pregnancy in an *in-vitro* fertilization programme after ovarian stimulation and gonadotrophin-releasing hormone and gonadotrophins. Hum Reprod. 1997; 12(11): 2515 – 2518.
11. Gonen Y, Casper RF. Prediction of implantation by the sonographic appearance of the endometrium during controlled ovarian stimulation for *in vitro* fertilization (IVF). J In Vitro Fert Embryo Transf. 1990; 7(3): 146 – 152.
12. Check JH, Nowroozi K, Choe J, Dietterich C. Influence of endometrial thickness and echo patterns on pregnancy rates during *in vitro* fertilization. Fertil Steril. 1991; 56(6): 1173 – 1175.
13. Check JH, Lurie D, Dietterich C, Callan C, Baker A. Adverse effect of a homogeneous hyperechogenic endometrial sonographic pattern, despite adequate endometrial thickness on pregnancy rates following in-vitro fertilization. Hum Reprod. 1993; 8(8): 1293 – 1296.
14. Ueno J, Oehninger S, Brzyski RG, Acosta AA, Philput CB, Muasher SJ. Ultrasonographic appearance of the endometrium in natural and stimulated *in-vitro* fertilization cycles and its correlation with outcome. Hum Reprod. 1991; 6(7): 901 – 904.
15. Dickey RP, Olar TT, Curole DN, Taylor SN, Rye PH. Endometrial pattern and thickness associated with pregnancy outcome after assisted reproduction technologies. Hum Reprod. 1992; 7(3): 418 – 421.
16. Serafini P, Batzofin J, Nelson J, Olive D. Sonographic uterine predictors of pregnancy in women undergoing ovulation induction for assisted reproductive treatments. Fertil Steril. 1994; 62(4): 815 – 822.
17. Bustillo M, Krysa LW, Coulam CB. Uterine receptivity in an oocyte donation programme. Hum Reprod. 1995; 10(2): 442 – 445.
18. Hock DL, Bohrer MK, Ananth CV, Kemmann E. Sonographic assessment of endometrial pattern and thickness in patients treated with clomiphene citrate, human menopausal gonadotropins, and intrauterine insemination. Fertil Steril. 1997; 68(2): 242 – 245.
19. Templeton A, Morris JK. Reducing the risk of multiple births by transfer of two embryos after *in vitro* fertilization. N Engl J Med. 1998; 339(9): 573 – 577.
20. Schieve LA, Peterson HB, Meikle SF, Jeng G, Danel I, Burnett NM, Wilcox LS. Live-birth rates and multiple-birth risk using *in vitro* fertilization. JAMA. 1999; 282(19): 1832 – 1838.
21. Alborzi S, Momtahan M, Zolghadri J, Parsanezhad ME. The effect of endometrial pattern and thickness on pregnancy rate in controlled ovarian hyperstimulation – intrauterine insemination. MJIRl. 2005; 19(3): 189 – 193.
22. Sharara FI, Lim J, McClamrock HD. Endometrial Pattern on the Day of Oocyte Retrieval Is More Predictive of Implantation Success than the Pattern or Thickness on the Day of hCG Administration. J Assist Reprod Genet. 1999; 16(10): 523 – 528.
23. Dede H, Dilbaz S, Demir B, Çınar Ö, Dede S, Göktolga Ü. The effect of endometrial thickness and pattern on pregnancy outcome in IVF/ICSI cycles. GJMMS. 2015; 1(2): 1 – 6,
24. Mercé LT, Barco MJ, Bau S, Troyano J. Are endometrial parameters by three-dimensional ultrasound and power Doppler angi outcome? Fertil Steril. 2008; 89(1): 111 – 117.
25. Rashidi BH, Sadeghi M, Jafarabadi M, Shahrokhi Tehraninejad E. Relationships between pregnancy rates following *in vitro* fertilization or intracytoplasmic sperm injection and endometrial thickness and pattern. Eur J Obstet Gynecol Reprod Biol. 2005; 120(2): 179 – 184.