

Similar Pregnancy Rates Between Different Endometrial Echo Patterns in ART

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OBJECTIVE: To determine whether endometrial echo pattern effects outcome in ART cycles

STUDY DESIGN : Prospective evaluation of 63 ART cycles results with the same protocole

RESULTS : The data from a total 63 patients were analyzed. The mean age of patients was 31.3 ± 5.1 . The mean number of oocytes retrieved was 8.9 ± 3.9 and the mean number of embryos transferred was 3.4 ± 0.5 . The overall clinical pregnancy rate was 33.3 % (21/63). In the sonographic evaluation of these 63 patients 37(58.7%) had homogeneous hyperechogenic (HH) pattern, 26 (33.3%) had non- HH pattern on the third day of embryo transfer.

CONCLUSION: As the morphological assessment of endometrium by sonography has a high inter observer variability and the influence of sonographic patterns of endometrium on pregnancy rates remains unclear, we conclude that evaluating endometrial patterns by sonography alone is not an optimal diagnostic procedure for determining the success of IVF outcome.

Key Words: Echo pattern, Infertility, ART, Pregnancy rate

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Introduction

It is well known that there are multiple factors necessary for successful implantation in invitro fertilization (IVF) programs. These include the age of the patients, the quality of the embryos and the quality of the endometrium.¹⁻³ Transvaginal ultrasound is a noninvasive technique which has been used to assess clinical parameters of uterine receptivity.¹⁻⁶ Although endometrial thickness and morphology are commonly assessed during IVF, the clinical significance of observed sonographic features remains unclear. Many studies have suggested that there is a significant correlation between the outcome of assisted reproductive treatment and endometrial thickness and morphology^{1,4,6} where as others have not confirmed such a relationship.⁶⁻⁹ The different results among these reports may be due to differences in study design ,population selection, the method of sonographic assessment and the protocols of stimulation.

In this study our aim was to evaluate the role of endometrial thickness and echo pattern in the outcome of assisted reproductive treatment.

Material and Method

We prospectively evaluated 63 patients who underwent IVF embryo transfer cycles in our department. Ultrasound scanning of the endometrium was done with a 7.5 MHZ transvaginal transducer (Combison 310 A Kretz Technique made in Austria) by one sonographer. On the day of human chorionic gonadotrophin (hCG) injection and the third day of embryo transfer, the maximum thickness of the endometrium as the maximum distance between each myometrial /endometrial interface through the central longitudinal axis of the uterus was measured. On the third day of embryo transfer the endometrial echogenicity patterns were visualized sonographically. The endometrial echogenicity patterns were classified in to two groups. A homogeneous hyperechogenic(HH) pattern was described as a single hyperechoic layer. Other patterns named as non-HH.

One cycle in which the women was aged ≤ 40 years and had at least three embryos transferred were included in the analysis to control for the confounding factors of age and embryo quality. Only the first cycle per patient was included to assure the independent of observations.

All patients underwent controlled ovarian hyperstimulation using a long protocol of SC leuprolide acetate (Lupron: Abbott pharmaceutical and human menopausal gonadotrophin (hMG) (Humegon: Organon). HCG was administered (10000 IU) when the estradiol concentration was approximately 200 pg/ml per follicle >16 mm in diameter and in the presence of more than three follicles >20 mm in diameter. Oocyte retrieval

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was carried out vaginally under sonographic guidance and local anesthesia. Embryo transfer was performed if the patient demonstrated adequate endometrial development on the day of hCG administration (endometrial thickness ≥ 8 mm).

Parameters relevant to the IVF cycle including number of oocytes retrieved, number of embryos transferred, serum estradiol and progesterone concentrations on the day of hCG administration and on the third day of embryo transfer, endometrial thickness and echo pattern and conception outcome were recorded for each patient.

All data were entered in to a computer using a SPSS statistical package for data analysis. The relationship between the variables and IVF outcome was investigated using students' t-test and chi-square test. A p-value <0.05 was considered to be statistically significant.

Results

The data from a total 63 patients were analyzed. The mean age of patients was 31.3 ± 5.1 (Range 21-40). The mean number of oocytes retrieved was 8.9 ± 3.9 and the mean number of embryos transferred was 3.4 ± 0.5 . The overall clinical pregnancy rate was 33.3 % (21/63). In the sonographic evaluation of these 63 patients 37(58.7%) had homogeneous hyperechogenic (HH) pattern, 26 (33.3%) had non- HH pattern on the third day of embryo transfer.

The pregnancy rates according to the endometrial echo pattern on the third day of embryo transfer are seen in Table 1. Although the pregnancy rates were higher in the HH group than the non-HH group that did not reach statistical significance. (37.8% for HH type and 26.9% for non-HH type; P=NS).

Table 1: The relationship between the endometrial echo patterns on the third day of embryo transfer and conception rates

	HH* (n=37)	Non-HH (n=26)
Conception cycle (n=21)	14 (37.8%)	7 (26.9%)
Non-conception cycle (n=42)	23 (62.2%)	19 (73.1%)

*Homogeneous hyperechogenic pattern

The data on stimulation parameters and IVF outcome are given in Table 2. There were no statistically significant differences in age, number of oocytes retrieved, number of embryos transferred, indication of IVF, serum hormone concentrations on the day of hCG administration and on the third day of embryo transfer between conception and non conception cycles. Similarly there was also no statistical difference in endometrial thickness (on the day of hCG administration in the group of patients who achieved pregnancy and in those who did not (10.1 ± 1.2 mm for conceiver and 9.8 ± 1.6 mm for non-conceivers; p=NS).

Table 2: Comparison of stimulation characteristics between conception and non conception cycles

	Conception cycles (n=21)	Non-conception cycles (n=42)
Oocytes retrieved (n)	9.7 \pm 3.7	8.6 \pm 4.0
Embryos transferred(n)	3.6 \pm 0.6	3.3 \pm 0.5
On the day of hCG administration		
Estradiol(pg/ml)	1884.3 \pm 1012.1	2069.5 \pm 1136.5
Progesterone(ng/ml)	1.1 \pm 0.5	1.1 \pm 0.5
Endometrial thickness(mm)	10.1 \pm 1.2	9.8 \pm 1.6
On the third day of embryo transfer		
Estradiol(pg/ml)	1140.3 \pm 853.1	878.5 \pm 558.1
Progesterone(ng/ml)	34.9 \pm 11.3	32.9 \pm 11.5
Endometrial thickness(mm)	11.4 \pm 1.9	10.7 \pm 2.7
Age(years)	30.2 \pm 5.5	31.9 \pm 4.7
Infertility factors n (%)		
Tubal	3 (14.3 %)	5 (11.9 %)
Endometriosis	1 (4.8 %)	2 (4.8 %)
Male	9 (42.9 %)	20 (47.6 %)
Multiple	6 (28.6 %)	12 (28.6 %)
Unexplained	2(9.5 %)	3 (7.1 %)

The comparison of stimulation characteristics between the echo patterns on the third day of embryo transfer is seen on Table 3.

Table 3: Comparison of stimulation characteristics between the echo patterns on the third day of embryo transfer

	HH* (n=37)	Non-HH (n=26)
Oocytes retrieved (n)	9.0 \pm 3.8	8.9 \pm 4.2
Embryos transferred(n)	3.4 \pm 0.5	3.4 \pm 0.6
On the day of hCG administration		
Estradiol(pg/ml)	2051.8 \pm 1138.6	1945.1 \pm 1040.7
Progesterone(ng/ml)	1.1 \pm 0.5	1.1 \pm 0.5
Endometrial thickness(mm)	10.1 \pm 1.3	9.7 \pm 1.5
On the third day of embryo transfer		
Estradiol(pg/ml)	1099.0 \pm 736.2	776.0 \pm 535.9
Progesterone(ng/ml)	35.8 \pm 9.6	30.4 \pm 13.1
Endometrial thickness(mm)	11.0 \pm 2.7	10.9 \pm 2.1
Age(years)	30.9 \pm 4.6	31.9 \pm 5.6
Infertility factors n (%)		
Tubal	5 (13.5 %)	3 (11.5 %)
Endometriosis	2 (5.4 %)	1 (3.8 %)
Male	16 (43.2 %)	13 (50 %)
Multiple	11 (29.7 %)	7 (26.9 %)
Unexplained	3 (8.1 %)	2 (7.1 %)

There were no statistically significant differences in age, number of oocytes retrieved, number of embryos transferred, indication of IVF, serum hormone concentrations on the day of hCG administration and on the third day of embryo transfer between HH and non-HH groups. Likewise there was also no statistical difference in endometrial thickness (on the day of hCG administration) between HH and non-HH groups. (10.1±1.3 mm for HH group and 9.7±1.5 mm for non-HH group; p=NS).

In the HH group two spontaneous abortions occurred. There were no abortions in the non-HH group.

Discussion

Embryo implantation is an important step in the success of IVF programme. Uterine receptivity is one of the factors that may affect the implantation process. Endometrial thickness and echo patterns were reported as clinical parameters of uterine receptivity.⁶⁻⁹ In a study by Grunfeld et al,¹⁰ the midluteal phase sonogram of the endometrium demonstrated a sensitivity of 100 % and a specificity of 62% for the detection of histologically normal endometrial development. However, Sterzik et al¹¹ found no significant histological differences between the different sonographic patterns.

Although many studies have suggested that endometrial thickness and echogenicity pattern correlate with implantation and pregnancy rate, a consensus about this relationship has not been reached.

Dickey et al¹ found that fecundity was increased when the endometrium was at least 9mm thick. Noyes et al⁵ evaluated 516 IVF cycles and found pregnancy and ongoing pregnancy rates to be higher when the endometrial thickness was ≥ 9 mm. Similarly Khalifia et al⁶ reported that minimal endometrial thickness of 7-8 mm is required to establish a clinical pregnancy after IVF/embryo transfer. Kovacs et al¹² analyzed 1228 IVF/ICSI cycles retrospectively and they concluded that increased endometrial thickness on the day of transfer was associated with higher pregnancy rates. Likewise in a study conducted by Rinaldi et al¹³ a minimum thickness of 10 mm during IVF was found to produce a higher pregnancy rate. However in the other published studies no significant association between endometrial thickness and pregnancy outcome was seen.^{14,15}

In a prospective cohort study 1186 infertile women were evaluated and the authors concluded that the pregnancy rates of assisted reproductive procedures were influenced only marginally by the degree of endometrial proliferation.¹⁴ Likewise many studies concluded that endometrial thickness at time of hCG administration had only marginal prognostic value when only the extremes of poor growth were seen.^{8,16,17} With respect to these findings, as our aim was not to determine a minimum

cutoff value of endometrial thickness to establish a pregnancy patients with inadequate development (endometrium thickness ≤ 8 mm) were not included in our study. By excluding the patients with inadequate endometrial development we were able to demonstrate that once the endometrium attains a threshold thickness whether increasing endometrial thickness always lead to increase in pregnancy rates or not. In this prospective study our data did not show a statistically significant difference between the endometrium thickness (Both on the day of hCG administration and on the third day of embryo transfer) in those patients who achieved pregnancies and versus those who did not. Our findings are in accordance with the results described by Bassil¹⁵ in 2001 for endometrial thickness. They reported that there were no significant differences in endometrial thickness in conception compared to non-conception cycles.

In 2000 Check et al¹⁸ reported that non-homogeneous hyperechogenic pattern 3 days after embryo transfer was associated with lower pregnancy rates. In 2003 the same authors evaluated midluteal phase echo patterns in 296 infertile women not taking follicle-maturing drugs. They concluded that failure to demonstrate a homogeneous hyperechogenic sonographic echo pattern by the midluteal phase was associated with decreased fecundity.¹⁹ In a prospective study which 175 patients were included transvaginal sonography was performed 15 hours before hCG administration and the endometrial echo pattern was assessed. The authors concluded that in patients receiving menotropins a homogeneous pattern was a bad prognostic sign regardless of endometrial thickness.¹⁷ However Chemiczky et al²⁰ reported that luteal endometrial morphology was not a sharp instrument to detect differences between women who did and who did not become pregnant following IVF treatment, while ovarian function as measured by hormonal markers, seemed to be a more reliable prognostic factor for IVF treatment outcome. In a prospective controlled study endometrial thickness, width, length, growth and pattern were assessed during the follicular and early luteal phases and the authors concluded that endometrial features as assessed by transvaginal ultrasound did not provide significant prognostic information with regard to the outcome of in vitro fertilization.¹⁵

For the evaluation of effect of endometrial echo patterns on pregnancy rates confounding factors such as age, number of embryos transferred, infertility factors and stimulation protocols should be standardized. In our study population both HH and non-HH groups were similar in terms of age, number of embryos transferred, IVF indications, serum hormone levels and treatment protocols. Likewise there were no statistically significant differences between conception and non-conception groups in terms of age, number of embryos transferred, IVF indications, serum hormone levels and treatment

protocols. In this present study we evaluated the relationship between echo patterns on the third day of embryo transfer and pregnancy rates. Although the pregnancy rates were higher in the HH group than the non-HH group that did not reach statistical significance. (37.8% for HH type and 26.9% for non-HH type).

As the morphological assessment of endometrium by sonography has a high inter observer variability and the influence of sonographic patterns of endometrium on pregnancy rates remains unclear, we conclude that evaluating endometrial patterns by sonography alone is not an optimal diagnostic procedure for determining the success of IVF outcome.

ART Sikluslarında Değişik Endometrial Eko Paternlerinde Benzer Gebelik Oranları

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Endometrial ekopaternalinin ART sikluslarında sonuçlar üzerindeki etkisini araştırmayı amaçladık.

Bu çalışmada prospektif olarak 63 aynı protokol uygulanan hastaların sonuçları incelenmiştir.

Hastaların ortalama yaşları 31.3 ± 5.1 'idi. Ortalama elde edilen oosit sayısı 8.9 ± 3.9 ve ortalama transfer edilen embriyo sayısı 3.4 ± 0.5 olarak bulundu. Toplam klinik gebelik oranı 33.3 % (21/63) idi. Embriyo transferi üçüncü günde 63 hastanın sonografik incelenmesinde 37 hastada (58.7) homojen hiperekojenik (HH) patern, 26 hastada (33.3) ise non-HH patern olarak bulundu.

Endometriumun sonografi ile morfolojik değerlendirilmesi yüksek inceleyiciler arası değişkenliğe sahiptir ve endometriumun sonografik paternlerinin gebelik üzerine etkileri halen net değildir. Sonuç olarak USG ile tesbit edilen eko paternleri IVF başarısını öngörmeye tek başına yeterli olmadığı tesbit edilmiştir.

Anahtar Kelimeler: Eko patern, İnfertilite, Yardımcı üreme teknikleri, Gebelik oranları

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