

# A Two-year Cross-sectional Prospective Study for Assessment of Endometrial Thickness and Volume using Three-dimensional Transvaginal Ultrasound among *in vitro* Fertilization Patients of Royan Institute in Iran

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## ABSTRACT

**Introduction:** To evaluate the role of endometrial thickness and volume using three-dimensional transvaginal ultrasound (3-D TVUS) in order to predict pregnancy outcome in assisted reproductive technology (ART) cycle on the day of human chorionic gonadotropin (hCG) administration.

**Materials and methods:** In this prospective study, the long protocol of controlled ovarian hyperstimulation was prescribed for women. Endometrial thickness and volume were measured using the 3-D TVUS, for 166 women undergoing ART cycle, on the day of hCG administration at Royan Institute, Tehran, Iran, between 2009 and 2011. All patients were divided into three groups. Regarding endometrial thickness, there are three groups as follows: Group I:  $\leq 7$  mm, group II: 7–14 mm, and group III:  $> 14$  mm; all patients were also divided into three groups according to endometrial volume calculated as follows: Group IV:  $< 2$  cc, group V: 2–4.5 cc, group VI:  $> 4.5$  cc. Pregnancy rate (PR) was compared between all groups.

**Results:** A total of 166 patients were analyzed. Overall PR was 39.8% after *in vitro* fertilization (IVF). Participant's age ranged from 20 to 38 years old with the mean age of  $29.9 \pm 4.23$ . No significant cut-off value was found for endometrial thickness and volume.

**Conclusion:** Endometrial thickness and volume on the day of hCG are significant in limited value and in a clinical setting for predicting implantation in ART cycle.

**Keywords:** Endometrial thickness, Endometrial volume, Ultrasonography.

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## INTRODUCTION

Assisted reproductive treatment (ART) cycle is considered as an expensive procedure with low implantation and pregnancy rate (PR); therefore, assessment of predictors of success in women with ART cycle is important. Successful implantation after ART is attained through good embryo quality and receptive endometrium.<sup>1,2</sup> Endometrial receptivity depends on endometrial thickness, volume, and ecopattern, which all could be detected by transvaginal ultrasound (TVUS).

There is still controversy about the predictive value of endometrial thickness and volume in outcome of *in vitro* fertilization (IVF) treatment. Several studies demonstrated significant correlation between PR and endometrial thickness,<sup>2,3,5-7</sup> whereas others did not show such a relationship,<sup>4,8-11</sup> indicating that the endometrial thickness does not reliably predict the probability of pregnancy.

Three-dimensional TVUS (3-D TVUS) is considered to be one of the best noninvasive routine procedures of clinical investigation in ART cycle by which the endometrial parameters (thickness, volume, and ecopattern) are assessed. With the advent of 3-D TVUS, it is possible to perform reliable volume calculations and to assess the data as predictive parameters for PR after ART.

The objective of the current study was to investigate the role of endometrial thickness and volume in IVF outcome (PR). This study sought to determine whether a thickened endometrium with more volume on the day of human chorionic gonadotropin (hCG) were predictive of PR in ART patients in a sample of Iranian infertile ladies.

## MATERIALS AND METHODS

A total of 166 patients with IVF cycle resulting in embryo transfer (ET) were recruited for this prospective study.

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Data sampling was done based on the quality not grouping and based on previous articles, analyzed by grouping, so that, there is no statistically significant difference between endometrial parameters and pregnancy outcome. The subjects were diagnosed with primary or secondary infertility for various etiologies like tubal, male, endometriosis, polycystic ovary syndrome, and unexplained factors. Evaluation of endometrial thickness and volume on the day of hCG administration was performed at Royan Institute between 2009 and 2011. The mean age of study population was  $29.9 \pm 4.23$  years.

Only women with the age of "38 years old, body mass index"  $35 \text{ kg/m}^2$ , absence of uterine pathologies (such as polyp, mullerian anomalies, endometrial hyperplasia, and fibroma with compressor effect), with no history of uterine surgery and first IVF cycle were included in the study. All patients were divided into three groups, according to endometrial thickness calculated, as follows: Group I with endometrial thickness  $\leq 7$  mm, group II with endometrial thickness of 7 to 14 mm, and group III with endometrial thickness  $> 14$  mm. Furthermore, all patients were divided into another three groups, according to endometrial volume calculated, as follows: Group IV with endometrial volume  $< 2$  cc, group V with endometrial volume of 2 to 4.5 cc, and group VI with endometrial volume  $> 4.5$  cc. The conventional long protocol with gonadotropin-releasing hormone agonist (GnRHa) was used for ovarian stimulation in all cycles. All patients received oral contraceptive pill (OCP low dose) starting from the 5th day of their cycle that was followed by daily intracutaneous injection of  $500 \mu\text{g}$  GnRH till 21st day of cycle. Dose of the GnRHa with daily dose of  $112.5 \text{ IU/mL}$  follicle-stimulating hormone was started. Depending on the patient's age and infertility causes, dose of Gonal F ampule was variable and could be prescribed 3 ampules for each patient. All patients underwent serial ultrasound examination to assess follicular growth until at least five follicles with a mean diameter of 16 mm were seen. On the day of hCG administration, a 3-D TVUS was performed by single experienced radiologist (at least 13 years of performing sonography) using an Accuvix-Probe VD (3–8 MHz, Medison Co., South Korea).

### Endometrial Thickness Measurement

In longitudinal view of the uterus, endometrial thickness measurements were conducted from the outer edge of the endometrial-myometrial interface to the outer edge in the widest part of the endometrium. The measurement includes both layers of the endometrium (Fig. 1). In the presence of the fluid in the endometrial cavity, the largest



Fig. 1: Endometrial thickness measurement

anterior and posterior endometrial thicknesses should also be calculated separately.

### Endometrial Volume Measurement

In order to measure endometrial volume, by using three-dimensional extended imaging Virtual Organ Computer-aided Analysis (3DXI VOCAL) method, rotational slices are used. This XI VOCAL method measures the volume of an object in the selected reference images in multislice view mode by using parallel slices. Horizontal slices are used. The object is cut into numerous sectional slices to determine its volume (Fig. 2). The XI VOCAL was superior to the multiplanar and VOCAL method with 10 planes estimated volumes closest to the real volumes (Fig. 2).

Ethical approval had been sought and an informed written consent was obtained from all women. Observed differences were evaluated for statistical significance using the chi-square test. Level of significance was set at  $p < 0.05$ .

### RESULTS

The study includes a total of 166 patients. All patients underwent assessment of endometrial thickness and volume on the day of hCG administration. The overall PR was 39.8%. Participant's age ranged from 20 to 38-year-old and the mean age was  $29.9 \pm 4.23$ .

According to endometrial thickness, patients were divided into three groups. Table 1 shows the comparison of the PR among the women in three different groups of endometrial thickness (groups I–III). There is no statistical significance in sagittal thickness of endometrium and PR by using chi-square test ( $p = 0.6$ ) (Graph 1).

Table 2 depicts the comparison of PR among the women in three different groups of endometrial volume (groups IV–VI). There is no relationship in endometrial volume and PR ( $p = 0.22$ ) (Graph 2).

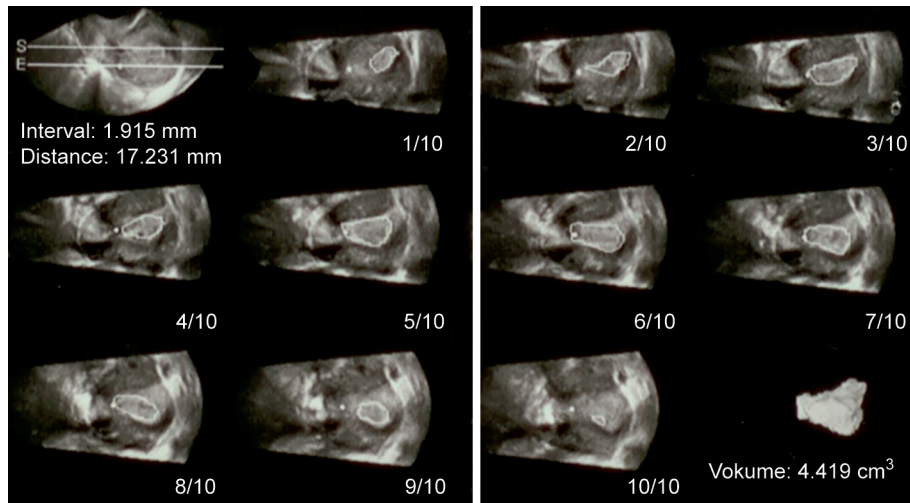


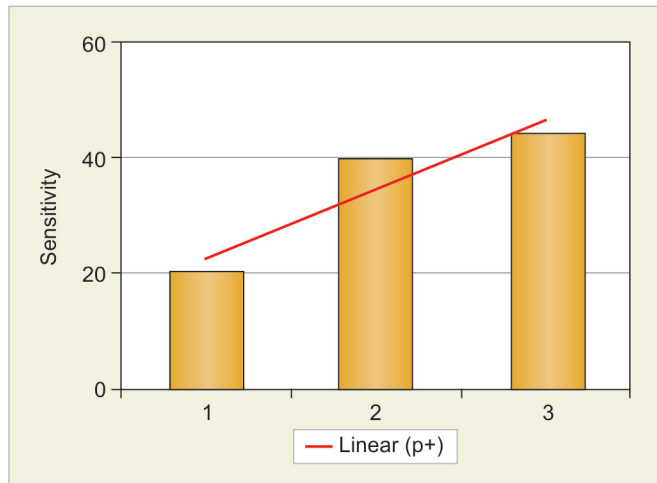
Fig. 2: Endometrial volume measurement

Table 1: Positive and negative pregnancy in three groups of endometrial thickness

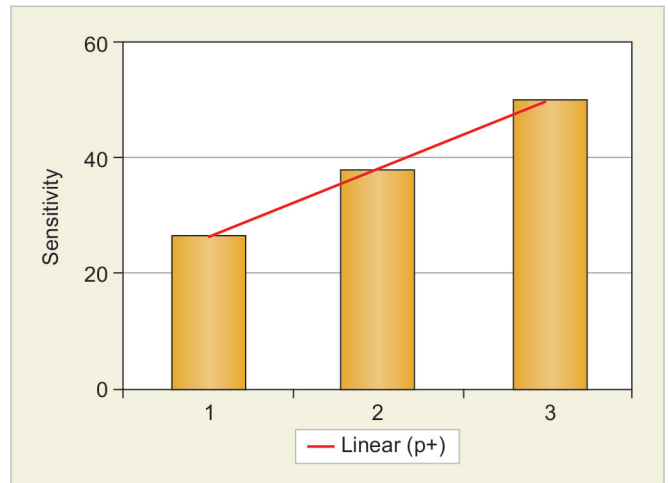
Groups of sagittal endometrial thickness (mm)	Positive pregnancy		Negative pregnancy		Total
	Number	Percent	Number	Percent	
	Group I	1	20	4	
Group II	54	39.7	82	60.3	136
Group III	11	44	14	56	25

Table 2: Positive and negative pregnancy in three groups of endometrial volume

Groups of endometrial volume (cc)	Positive pregnancy		Negative pregnancy		Total
	Number	Percent	Number	Percent	
	Group IV	4	26.7	11	
Group V	42	37.8	69	62.2	111
Group VI	20	50	20	50	40



Graph 1: Positive pregnancy rate (percent) among all three groups of endometrial thickness (groups I, II, and III)



Graph 2: Positive pregnancy rate (percent) among all three groups of endometrial volume (groups IV, V, and VI)

The tables show limited value of both parameters (endometrial thickness and volume) in prediction of pregnancy. Although there is no statistically significant relationship in positive PR and endometrial thickness and volume, likelihood ratio of pregnancy in groups III and VI is higher than others.

The findings showed that 39.8% were pregnant and 60.2% were not pregnant. Considering embryo quality, 166 patients had embryo quality of A and B (in order to avoid embryo quality as a confounder when analyzing

the predictive value of ultrasonographic parameters) (Table 3). According to chi-square test, there is no statistical significance between PR and embryo quality ( $p = 0.022$ ) (Table 3).

Table 3: Pregnancy rate according to embryo quality

Embryo quality	AB	Positive pregnancy		Negative pregnancy		Total
		Number	Percent	Number	Percent	
		66	39.8	100	60.2	166
						100



**Table 4:** Some data published about the role of 3-D ultrasound for predicting outcome in IVF program

Authors	Number	Primary outcome	3D method	Day 3-D TVUS	PR	Findings
Raga et al	72	PR	Multislice	Embryo transfer	29.2%	No pregnancy if endometrial volume < 1 mL. If endometrial volume $\geq$ 2 mL, no difference in PR
Schild et al	47	PR	Multislice	Oocyte retrieval	31.9%	No difference in endometrial volume between conception and nonconception cycles
Yaman et al	65	PR	Multislice	hCG	32.3%	No difference in endometrial volume between conception and nonconception cycles No pregnancy if endometrial volume < 2.5 mL

PR: Pregnancy rate; hCG: Human chorionic gonadotropin; 3-D TVUS: Three-dimensional transvaginal ultrasound

## DISCUSSION

Successful implantation in ART cycles depends on multiple factors, among which endometrial receptivity, such as endometrial thickness and volume detected by 3-D TVUS, is of importance. There has been considerable controversy concerning the value of endometrial thickness and volume in the prediction of endometrial receptivity. In our study, there were no significant differences regarding endometrial volume and thickness in patients who became pregnant as compared to those who did not become pregnant; this finding is in agreement with previous studies in which they found no predictive value of endometrial volume and thickness on IVF results.<sup>8-12</sup> Some studies have showed endometrial thickness on the day of ET as an important factor in predicting the outcome of IVF cycles,<sup>4-6</sup> whereas others have failed to show such relation. In addition, some studies have proposed that endometrial thickness on the day of hCG injection had no predictive value for conception in IVF/intracytoplasmic sperm injection cycles or not useful in predicting IVF outcome.<sup>2,7,9,10,13,14</sup> Furthermore, it has become widely accepted that a minimum endometrial thickness (6 mm) is necessary to achieve a pregnancy.<sup>2</sup>

Since cycle outcome can be related to quantitative parameter, such as endometrial volume, it seems that an endometrial volume >2 mL is a prerequisite for good endometrial receptivity. Raga et al<sup>15</sup> and Schild et al<sup>12</sup> reported that no pregnancy was achieved when endometrial volume was <1 mL. On the other hand, findings of some studies depicted that in endometrial volume >2 mL, there was no relationship between mean endometrial volume measured by 3-D TVUS and IVF outcome.<sup>8,15</sup> The results of previously conducted study are illustrated in Table 4.

All patients received hCG for stimulation, in order to eliminate the bias resulting from different stimulation medications and their different effects on endometrial proliferation. It is well agreed that embryo quality and endometrial receptivity play an important role in pregnancy outcome in IVF. In our study all transferred embryos were of grade A, B, or AB.

## CONCLUSION

In conclusion, the findings of the present study suggest that 3D volume estimation of the endometrium as well as analysis of endometrial thickening on the day of the hCG administration had no predictive value for conception in IVF cycles. It remains to be seen whether larger clinical studies could define a threshold value of endometrial volume and thickness.

Oocyte recovery and transfer of frozen embryos during subsequent cycle is needed when more receptive endometrial thickness and volume is detected by 3-D TVUS.

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## REFERENCES

1. Pope CS, Cook EK, Arny M, Novak A, Grow DR. Influence of embryo transfer depth on *in vitro* fertilization and embryo transfer outcomes. *Fertil Steril* 2004 Jan;81(1):51-58.
2. Friedler S, Schenker JG, Herman A, Lewin A. The role of ultrasonography in the evaluation of endometrial receptivity following assisted reproductive treatments: a critical review. *Hum Reprod Update* 1996 Jul-Aug;2(4):323-335.
3. Spandorfer SD, Arrendondo-Soberon F, Loret de Mola JR, Feinberg RF. Reliability of intraobserver and interobserver sonographic endometrial stripe thickness measurements. *Fertil Steril* 1998 Jul;70(1):152-154.
4. Alborzi S, Momtahan M, Zolghadri J, Parsanezhad M. The effect of endometrial pattern and thickness on pregnancy rate in controlled ovarian hyperstimulation-intrauterine insemination. *Med J Islamic Republic Iran* 2005 Nov;19(3):189-193.
5. Aboulghar MM, Al-Inany HG, Aboulghar MA, Serour GL, Mansour RT, Amin YM, Abou-Setta AM. Three dimensional endometrial volume versus endometrial thickness measurement in prediction of IVF/ICSI outcome. *Middle East Fertility Soc J* 2005;10(1):63-67.
6. Noyes N, Liu HC, Sultan K, Schattman G, Rosenwaks Z. Endometrial thickness appears to be a significant factor in embryo implantation in *in vitro* fertilization. *Hum Reprod* 1995 Apr;10(4):919-922.
7. Zhao J, Zhang Q, Wang Y, Li Y. Endometrial pattern, thickness and growth in predicting pregnancy outcome following 3319 IVF cycle. *Reprod Biomed Online* 2014 Sep;29(3):291-298.

8. Schild RL, Indefrei D, Eschweiler S, Van der Ven H, Fimmers R, Hansmann M. Three-dimensional endometrial volume calculation and pregnancy rate in an *in vitro* fertilization programme. *Hum Reprod* 1999 May;14(5):1255-1258.
9. Fleischer AC, Herbert CM, Sacks GA, Wentz AC, Entman SS, James AE Jr. Sonography of the endometrium during conception and nonconception cycles of *in vitro* fertilization and embryo transfer. *Fertil Steril* 1986 Sep;46(3):442-447.
10. Bassil S. Changes in endometrial thickness, width, length and pattern in predicting pregnancy outcome during ovarian stimulation in *in vitro* fertilization. *Ultrasound Obstet Gynecol* 2001 Sep;18(3):258-263.
11. Oliveira JBA, Baruffi RLR, 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. *Human Reprod* 1997 Nov;12(2):2515-2518.
12. Schild RL, Knobloch C, Dorn C, Fimmers R, van der Ven H, Hansmann M. Endometrial receptivity in an *in vitro* fertilization program as assessed by spiral artery blood flow, endometrial thickness, endometrial volume, and uterine artery blood flow. *Fertil Steril* 2001 Feb;75(2):361-366.
13. Momeni M, Rahbar MH, Kovanci E. A meta-analysis of the relationship between endometrial thickness and outcome of *in vitro* fertilization cycles. *J Hum Reprod Sci* 2011 Sep;4(3):130-137.
14. Yaman C, Ebner T, Jesacher K, Sommergruber M, Radner G, Tews G. Sonographic measurement of endometrium thickness as a predictive value for pregnancy through IVF. *Ultraschall Med* 2002 Aug;23(4):256-259 (German).
15. Raga F, Bonilla-Musoles F, Casañ EM, Klein O, Bonilla F. Assessment of endometrial volume by three-dimensional ultrasound prior to embryo transfer: clues to endometrial receptivity. *Hum Reprod* 1999 Nov;14(11):2851-2854.