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Original Research

High Endometrial Thickness Does not Affect IVF/ICSI Outcomes

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ABSTRACT

Objective: We examined the impact of thicker endometrium (>15 mm) on in vitro fertilization (IVF) outcomes by evaluating the rates of clinical pregnancy, ongoing pregnancy, and live birth.

Methods: Intracytoplasmic sperm injection procedures performed at a single IVF center were retrospectively examined. A total of 380 cases from patients aged between 19 and 39 years were included. The patients were divided into 2 groups according to their endometrial thickness (EMT) value determined using ultrasonography on the day of human chorionic gonadotropin administration.

Results: Embryo day was 5 in 78.4% of cases with EMT <15 mm and 3 in 89.8% of cases with EMT ≥ 15 mm (p<.001). In the group with EMT <15 mm, IVF outcomes were 61.5% clinical pregnancy, 54.7% ongoing pregnancy, and 49.0% live birth. In the group with EMT > 15 mm, IVF outcomes were 64.3% clinical pregnancy, 52.4% ongoing pregnancy, and 41.7% live birth. There was no significant difference between the groups in terms of clinical pregnancy, ongoing pregnancy, and live birth rates (p>.05). Determining the EMT cut-off value as 14 mm also did not yield significant results. Live birth was present in 47.4% of the cases. There were no statistically significant differences between the groups with and without live birth in terms of the variables examined.

Conclusion: There was no significant relationship between EMT and achieving a live birth through IVF. Nevertheless, conducting prospective and comprehensive studies on thicker endometrium may yield data that could be beneficial for IVF practitioners.

Keywords: Endometrium, IVF/ICSI, live birth rate, pregnancy

INTRODUCTION

Identifying the most suitable endometrium for a good embryo transfer has always been very important for in vitro fertilization (IVF) practitioners. The endometrium thickness in the proliferative phase of the menstrual cycle and provides the necessary environment for implantation of the embryo. Progesterone secreted after ovulation makes the endometrium suitable for embryo implantation. If pregnancy occurs after fertilization, progesterone continues to be secreted from the ovaries, and the endometrium continues to facilitate the development of embryo until the formation of placenta (1-3). Therefore, morphologically normal and receptive endometrium is essential for successful implantation in IVF treatment.

Detailed assessment of endometrial thickness (EMT) and endometrium patterns became possible with the use of ultrasonography (USG). Different views about the clinical importance of EMT are provided to patients who undergo IVF treatment owing to infertility. It has been suggested that hypoechoic endometrium is better than isoechoic endometrium or hyperechoic endometrium for embryo implantation.[4] However, the ideal EMT is still controversial. In most of the previous studies evaluating the effect of EMT on IVF outcomes, it was reported that a cut-off value of 6-8 mm could be used (1-3). When the clinical results after IVF and intracytoplasmic sperm injection (ICSI) were examined according to these cut-off values, it was found that the results were significantly more negative in cases with thinner EMT values in almost all the studies (5-16). However, in contrast to the unanimous opinion against thin endometrium, the number of studies investigating the role of thicker endometrium (>14 mm) is limited, and it remains controversial whether a thick endometrium can affect endometrial receptivity (17-22). Although there are studies showing that thicker endometrium positively (14,18) or negatively (17,19) impacts IVF outcomes, there are also various studies showing that thicker endometrium has no impact on IVF outcomes (23-26).

The impact of EMT on the success of IVF procedure is still unclear. When the endometrium is thinner than the previously defined cut-off values, transfers may be canceled confidently. However, when the endometrium is thicker (often taken as being >14 mm or >15 mm thick), there is still no consensus on whether the

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Table 1. Individual characteristics of participants

Characteristics	Endometrial thickness			*p*
	<15 mm (n=296)	≥15 mm (n=84)	Total (n=380)	
Age (year)	28.86±4.77	28.56±5.06	28.79±4.83	.618
Duration of infertility (year)	5 (1–24)	6 (1–22)	5 (1–24)	.276
Body mass index (kg/m^2)	26.24±2.68	26.64±1.90	26.33±2.53	.125
PCOS	278 (93.92%)	83 (98.81%)	361 (95.00%)	.088
Tubal factor	4 (1.35%)	0 (0.00%)	4 (1.05%)	.580
Unexplained	20 (6.76%)	1 (1.19%)	21 (5.53%)	.057
Other	2 (0.68%)	0 (0.00%)	2 (0.53%)	1.000
Endometrial thickness (mm)	10 (6–14)	16 (15–21)	11 (6–21)	<.001
E2 on hCG day (pg/mL)	2923 (616.8–8,320)	2995 (1023–9300)	2948 (616.8–9300)	.840
P on hCG day (ng/mL)	0.9 (0.1–4)	0.9 (0.09–3.1)	0.9 (0.09–4)	.553
M2	14.37±4.00	14.26±3.14	14.35±3.82	.785
Embryo transfer day				
2	1 (0.34%)	0 (0.00%)	1 (0.26%)	<.001
3	62 (20.95%)	67 (79.76%)	129 (33.95%)	
5	232 (78.38%)	17 (20.24%)	249 (65.53%)	
6	1 (0.34%)	0 (0.00%)	1 (0.26%)	
Freshcycles	296 (100.00%)	84 (100.00%)	380 (100.00%)	N/A
Clinical pregnancy	182 (61.49%)	54 (64.29%)	236 (62.11%)	.641
Ongoing pregnancy	162 (54.73%)	44 (52.38%)	206 (54.21%)	.703
Live birth	145 (48.99%)	35 (41.67%)	180 (47.37%)	.236

Data are presented as mean ± standard deviation or median (minimum–maximum) for continuous variables according to the normality of distribution and as frequency (percentage) for categorical variables.
E2, estradiol; hCG, human chorionic gonadotropin; M2, mature oocyte; N/A, not available; P, progesterone; PCOS, polycystic ovary syndrome.

transfer should be canceled. In this study, we aimed to examine the impact of thicker endometrium (>14 mm and >15 mm) on IVF outcomes based on the rates of clinical pregnancy, ongoing pregnancy, and live birth to help clinicians who encounter thicker endometrium in practice.

METHODS

ICSI procedures performed at the Kayseri Memorial IVF Center between 2019 and 2020 were retrospectively examined. Patients aged between 19 and 39 years were included in the study. Ethics approval was obtained from the institutional review board (approval number: 3, date: 16/01/2020). Verbal informed consent was obtained from all participants included in the study. Controlled ovarian hyperstimulation of the patients was performed using an antagonist protocol with recombinant follicle-stimulating hormone. When at least 3 follicles were ≥17 mm in size, maturation was induced using standard recombinant 250 µg dose of human chorionic gonadotropin (hCG) (Ovitrelle; Merck Group, Darmstadt, Germany). Oocyte pickup (OPU) was performed via transvaginal route under anesthesia at 36 h after hCG. Embryo transfer was performed on the third or fifth day after OPU. The patients were divided into 2 groups according to the EMT value determined by USG on the day of hCG administration (group A had EMT <15 mm and group B had EMT≥15 mm). The age of the patients, cause and duration of the patients' infertility, hormonal characteristics of the patients, other characteristics, and clinical outcomes of the participants were recorded.

Main Points:

- Ideal endometrial thickness (EMT) is important for implantation in IVF procedure.
- Previous studies have shown that 7-15 mm EMT is the most suitable range, but there are not enough studies showing the impact of EMT > 15 mm on pregnancy outcomes.
- In this study, it was shown that EMT > 15 mm does not have a negative impact on pregnancy outcomes.

Statistical Analysis

All analyses were performed on the Statistical Package for the Social Sciences, version 21 (IBM SPSS Corp.; Armonk, NY, USA). Q-Q and histogram plots were used to determine whether

Table 2. Summary of individual characteristics with regard to the presence of live birth

Characteristics	Live birth		*P*
	Absent (n=200)	Present (n=180)	
Age (year)	28.92±5.10	28.65 ± 4.52	.587
Duration of infertility (year)	5 (1–24)	5 (1 – 20)	.652
Body mass index (kg/m^2)	26.47±2.37	26.18 ± 2.70	.262
PCOS	192 (96.00%)	169 (93.89%)	.480
Tubal factor	2 (1.00%)	2 (1.11%)	1.000
Unexplained	8 (4.00%)	13 (7.22%)	.251
Other	1 (0.50%)	1 (0.56%)	1.000
Endometrial thickness (mm)	12 (6–21)	11 (6 – 19)	.095
E2 on hCG day (pg/mL)	3000 (616.8–8697)	2892.5 (919–9300)	.307
P on hCG day (ng/mL)	0.9 (0.09–4)	0.9 (0.1–3.1)	.820
M2	14.43±3.79	14.26±3.87	.648
Embryo transfer day			
2	1 (0.50%)	0 (0.00%)	.223
3	75 (37.50%)	54 (30.00%)	
5	124 (62.00%)	125 (69.44%)	
6	0 (0.00%)	1 (0.56%)	

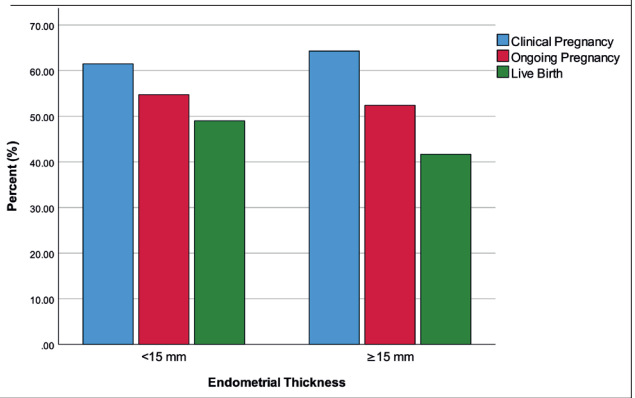
Data are presented as mean±standard deviation or median (minimum–maximum) for continuous variables according to the normality of distribution and as frequency (percentage) for categorical variables.

the variables were normally distributed. Data are presented as mean±standard deviation or median (minimum-maximum) for continuous variables according to the normality of distribution and as frequency (percentage) for categorical variables. Normally distributed variables were analyzed with independent samples *t*-test. Non-normally distributed variables were analyzed with the Mann-Whitney U test. Categorical variables were analyzed using the chi-square test or Fisher's exact test. P =.04 was considered statistically significant.

RESULTS

A total of 380 women aged 19-39 years with fresh embryo transfer were included in the study. The EMT on the day of hCG administration ranged from 6 to 21 mm. Embryo day was 5 in 78.4% of cases with EMT <15 mm and 3 in 89.8% of cases with EMT≥15 mm. There was a significant difference between the groups in terms of embryo day (p<.001). In the group with EMT <15 mm, IVF treatment results were as follows: 61.5% clinical pregnancy, 54.7% ongoing pregnancy, and 49.0% live births. In the group with EMT>15 mm, IVF outcomes were as follows: 64.3% clinical pregnancy, 52.4% ongoing pregnancy, and 41.7% live births (Figure 1). There was no significant difference between the groups in terms of clinical pregnancy, ongoing pregnancy, and live birth rates (p>.05) (Table 1). When the EMT threshold was accepted as 14 mm, we did not find any differences between the groups.Live birth was present in 47.4% of the cases. There was no statistically significant difference between patients who had live births and those who did not in terms of the variables examined (Table 2).

Figure 1. Pregnancy and live birth percentages with regard to endometrial thickness



DISCUSSION

Studies investigating whether EMT is a determinant for IVF-achieved pregnancy in the literature have reported controversial results. In this study, which was carried out to evaluate the effect of EMT on the clinical outcomes of IVF, it was found that the frequency of clinical pregnancy and live birth is not associated with whether the EMT values are <15 mm or >15 mm. There was also no relationship between EMT and IVF outcomes in terms of live birth.

Many studies have examined the relationship between EMT and IVF outcomes, and there are systematic reviews and meta-analyses evaluating the findings of these studies. In a recent and comprehensive meta-analysis examining the impact of EMT on IVF cycle outcomes, Gao et al.[1] showed that decreased EMT was significantly associated with decreased rates of implantation, pregnancy, ongoing pregnancy, and live birth. In another systematic review and meta-analysis examining the effect of EMT on pregnancy rate with IVF, Kasius et al. (2) reported that EMT was not tenable as a parameter to predict pregnancy with IVF. In addition, they showed that the possibility of pregnancy and live birth rate decreased in cases with EMT≤7 mm (2). In a similar meta-analysis by Momeni et al. (3), it was reported that the EMT of women who became pregnant with IVF was higher than that of women who did not become pregnant. In addition, they found that the mean EMT difference between the groups was <1 mm.[3] In many cohorts, randomized controlled trials, and cross-sectional studies, the suitability of EMT as a tool to predict IVF outcomes at certain cut-off points was studied, and the results were significant (5-22). In our study, no significant difference was found in

EMT values when cases grouped according to the presence or absence of live births were compared. Moreover, no significant difference was found between the 2 groups (i.e., cases with EMT <15 mm vs cases with EMT≥15 mm) in terms of IVF outcomes.

In previous studies, IVF outcomes were compared according to different EMT cut-off values. Our literature review found that a cut-off value between 6 and 8 mm was determined for EMT in most of these studies (1-3) Although few studies focused on the impact of higher EMT values (e.g., EMT≥15 mm) on IVF outcomes, there is no study showing the relationship between high EMT values and pregnancy rates (11, 17-22). Some studies reported that an EMT ≥15 mm decreases the frequency of clinical pregnancy (17). In contrast, in some other studies, it was reported that the frequency of clinical pregnancy increased significantly with higher EMT values (14, 18). Another study reported that the frequency of miscarriage was higher in cases with EMT≥15 mm (19). It was thought that the negative results for thicker EMT may be caused by mechanical trauma in thicker endometrium during embryo transfer. In a study examining the effect of EMT on the day of hCG administration, Bu and Sun (20) reported that in all 3 groups (poor, medium, and high responders), the prevalence of pregnancy was significantly higher in cases with an EMT >14 mm than in cases with lower EMT value. In a study conducted in Turkey, Bozdag et al. (21) found that an EMT >14 mm had a positive impact on IVF outcomes. In some studies, different EMT cut-off values, such as 12 mm (11, 27, 28) and 16 mm (14, 29), were determined, and positive or negative IVF outcomes were reported. In some other studies, patients were classified into 3 groups according to EMT values (2 cut-off values). The results showed a significant difference between the group with the highest EMT values and that with the lowest value in terms of pregnancy and live birth rate (30, 31). The results of our study, in contrast to those of the aforementioned studies, show that IVF outcome is not associated with EMT, indicating that 14 or 15 mm values for EMT cannot be used as cut-off thresholds to predict IVF outcomes. Singh et al. (11) suggested that the minimum value for EMT should be 5.8 mm for clinical pregnancy, and an EMT value between 8 and 10 mm was ideal. They stated that there may be an increasing and then decreasing relationship between a higher value of EMT and success of IVF, suggesting that the success of IVF could decrease at extreme values of EMT (11).The similarities in IVF outcomes between the studies that grouped patients according to the primary cut-off value of EMT (15 mm) and our study in which a secondary analysis for EMT cut-off value of 14 mm contradict most of the previous findings. With more comprehensive and standardized future studies on this subject, our results can be examined in more detail.

Although the retrospective design of our study, an important limitation, can be considered a factor that could skew results, other studies including meta-analysis, prospective studies or observational studies have obtained similar conclusions (2, 23-26). In the meta-analysis by Kasius et al. (2) it was concluded that pregnancy with IVF could not be predicted with EMT. Rashidi et al. (26) reported that there was no significant difference between the EMT values of pregnant women and those of non pregnant women who underwent IVF. Similarly, Dietterich et al. (22) found that there was no significant relationship between EMT and IVF outcomes. In a study conducted in Turkey, Kınay et al. (13) reported that EMT was not a determinant for the development of clinical pregnancy with IVF.

CONCLUSION

Although there are conflicting views in the literature on whether EMT has a positive or negative impact on IVF outcomes (given that it is often accepted when it is above a certain threshold, such as 6 mm), it was generally suggested that lower EMT values would negatively impact IVF outcomes. In our study, we determined that there is no significant relationship between EMT and achieving a live birth with IVF when the patients were divided into two groups based on a 15 mm cut-off value. Determining the EMT cut-off value as 14 mm also did not yield any significant role in the prediction of IVF outcomes. Further prospective and comprehensive studies on thicker endometrium should be conducted in future to guide IVF practitioners on this matter.

Ethics Committee Approval: Ethics committee approval was received for this study from the institutional review board of Memorial Hospital (Approval date: 16.01.2020, No: 3).

Informed Consent: Verbal informed consent was obtained from all participants.

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