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Original Article

Relationship between thickness and pattern of endometrium and pregnancy rate in in vitro fertilization-intracytoplasmic sperm injection cycles

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Abstract

Introduction: Assisted reproductive treatment (ART) cycle like in vitro fertilization-intracytoplasmic sperm injection (IVF-ICSI) is an expensive procedure with low implantation and pregnancy rate. Endometrial pattern and thickness are suggested as the factors of endometrial receptivity and predictors of IVF-ICSI success. The correlation between endometrial pattern and thickness with pregnancy rate in IVF-ICSI cycles was evaluated in this study.

Methods: In this study, 150 patients with 150 cycles were included. Ovulation induction was performed by antagonist protocol and in the day of human chorionic gonadotropin (HCG) administration, thickness and pattern of endometrium were measured by transvaginal sonography. Two weeks after embryo transfer, pregnancy rate was defined by blood HCG and the correlation between pregnancy rate with thickness and pattern of endometrium in the day of HCG administration was evaluated.

Results: Pregnancy rate in triple line pattern (TLP) was significantly higher than homogenous hypoechoic pattern (P = 0.006). Endometrium thickness was significantly higher in cases of pregnancy (P < 0.001). Sensitivity and specificity of endometrium thickness > 9.5 mm in predicting pregnancy rate was 77.50% and 77.50%, respectively. In addition, the sensitivity and specificity of TLP alone or combined with endometrium thickness were 87.50%, 35.45%, 67.50% and 80.90%, respectively.

Conclusion: Thickness and pattern of endometrium both could predict pregnancy occurrence. Having TLP along with endometrium thickness > 9.5 mm, the possibility of pregnancy following IVF-ICSI increases.

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Introduction

Assisted reproductive treatments (ART) have been used for treatment of infertility. Despite technical advances, the implantation rate is still low. High procedure expenses with low implantation and pregnancy rate in in vitro fertilization-intracytoplasmic sperm injection (IVF-ICSI) has emerged the need to identify the factors predicting the procedure success.[1,2]

Embryo quality and endometrial receptivity are two important factors of ART cycle success. Identifying the factors affecting the endometrial receptivity could improve the outcome.[3] With proper hormonal and structural basis, endometrium will grow to appropriate thickness and would be suitable for embryo implantation.[4] Different studies have evaluated endometrial pattern and thickness as factors of endometrial receptivity and predictors of IVF-ICSI success.[5-12] Some studies have shown that suitable thickness for implantation is between 7-14 mm and the likelihood of pregnancy is decreased in values below and above this rate. In contrast, some studies were unable to show any correlation between endometrial thickness and pattern

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with implantation and pregnancy rate.[2,13-16]

There is no definite endometrial thickness in which IVF-ICSI cycle would increase the pregnancy rate. In this study, we evaluated the correlation between endometrial pattern and thickness with pregnancy rate in IVF-ICSI cycles.

Methods

In this cross-sectional study, 150 patients with 150 IVF-ICSI cycles admitted to Al-Zahra hospital, Tabriz, Iran, were examined between December 2014 and January 2017. All fresh IVF or ICSI treatment cycles that used gonadotropin-releasing hormone (GnRH) antagonist administration as the method of ovarian stimulation and reached oocyte pick up and embryo transfer within the study period were included, regardless of diagnosis, reproductive history, or insemination method. Cycles using donor oocytes or cryopreserved embryos were excluded from this study. Women with known intrauterine anomalies or history of abortion, dilatation and curettage (D and C), treatment hysteroscopy, polypectomy, myomectomy or septum resection were excluded. Patients underwent no therapeutic interventions except routine procedures. The study was approved by the ethics committee of Tabriz University of Medical Sciences.

All participants were treated with GnRH antagonist protocol. Patients received recombinant human follicle stimulating hormone Follitropin Alfa (Gonal-F) (150-225 IU, subcutaneously) and human menopausal gonadotropin (hMG) 75-150 IU from day 2-3 of menstruation. Serial trans-vaginal sonography was performed. When the mature follicle (≥ 13.0 mm) was detected, GnRH antagonist (Cetrotide) (0.25 mg/day, subcutaneously) was injected. Triggering was started with 10000 IU human chorionic gonadotropin (HCG) (Pregnyl, Organon, Netherland) when at least three follicles with a mean diameter of 18.0 mm was observed. 36 hours after HCG injection, oocytes were punctured and embryo transfer was performed three days later. The pregnancy test (serum βHCG) was performed two weeks after embryo transfer.

Endometrial thickness was defined as the maximal distance between the echogenic interfaces of the myometrium and the endometrium and was measured in the mid-sagittal plane by two dimensional transvaginal ultrasound on the day of HCG administration. Endometrial pattern was classified as pattern A, pattern B, or pattern C as a triple-line pattern consisting of a central hyperechoic line surrounded by two hypoechoic layers, an intermediate isoechogenic pattern with the same reflectivity as the surrounding myometrium and a poorly defined central echogenic line, as homogenous, hyperechogenic endometrium, respectively.

All data were analyzed using SPSS (version 17, SPSS Inc., Chicago, IL, USA). Results are expressed as mean ± standard deviation (SD) or percentage. The chi-square and Fisher exact tests were used to compare categorical variables. Receiver operating curve (ROC) and area under curve (AUC) were used to define cut-off point and for endometrial thickness in predicting pregnancy rate, respectively. Sensitivity and specificity of endometrial thickness alone and in line with endometrial pattern was calculated. The P values of less than 0.050 were considered statistically significant.

Results

A total of 150 women with 150 IVF-ICSI cycles were studied. The mean age of patients and the mean duration of infertility was 31.70 ± 6.58 and 6.12 ± 4.72 years, respectively. 126 (84.0%) and 24 (16.0%) of subjects suffered from the primary and secondary infertility, respectively. Causes of infertility were combined, male factor, tubal factors, and unexplained with rates of 51.3%, 29.3%, 17.3%, and 2.0%, respectively.

Mean endometrial thickness was 9.14 ± 1.60 (ranging 6-14 mm). Endometrial pattern was type A and type B among 106 (70.7%) and 44 (29.3%) of patients, respectively.

40 (26.7%) of patients had positive pregnancy tests. Positive pregnancy test was significantly higher in type A endometrial pattern than type B with 33.0% and 11.3%, respectively (P = 0.006). In addition, cases with positive pregnancy test had significantly higher endometrial thickness compared to the negative ones with 10.75 ± 1.67 and 8.56 ± 1.11, respectively (P < 0.001). All pregnancy cases occurred in thicknesses between 9.0-14.0 mm.

Figure 1 shows the ROC with the AUC of 0.876 (P < 0.001) which yields to a cut-off value of 9.5 mm. Dividing the patients into groups with endometrial thickness < 9.5 and ≥ 9.5, pregnancy rate was significantly higher in the second group as 53.4% and 9.8%, respectively (P < 0.001). With a cut-off of 9.5 mm, the sensitivity and specificity of endometrial thickness in predicting positive pregnancy was 77.5% and 75.5%, respectively.

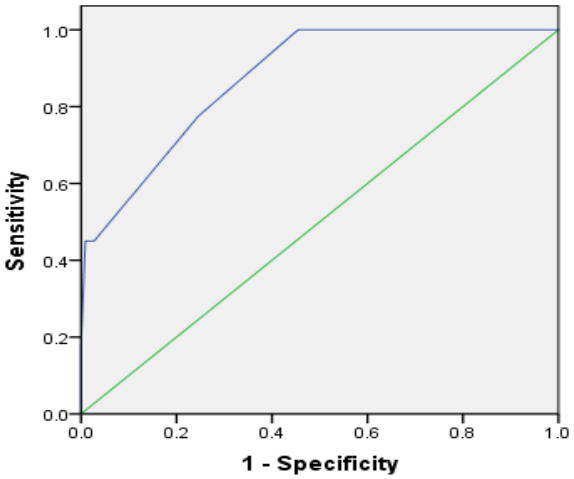

Figure 1. Receiver operating characteristic (ROC) curve for the predictive value of endometrial thickness for positive pregnancy test

Sensitivity, specificity, positive and negative predictive values of different endometrial thickness and endometrial pattern were evaluated alone or in combination with the endometrial thickness (Table 1). The highest sensitivity was obtained for endometrial thickness > 7.0 mm, however with the lowest specificity. The highest specificity were noted for endometrial thickness > 9.5 mm alone or in line with type A endometrial pattern.

Discussion

Achieving a proper endometrial thickness is important for successful infertility treatment. Proper endometrial thickness and pattern affects implantation rate and consequently increases the clinical pregnancy rate.[17,18]

In this study, the correlation between endometrial thickness and pattern with pregnancy rate was evaluated in IVF-ICSI cycles. The pregnancy rate was 26.7%, in addition, the most successful pregnancies had high endometrial thickness and type A (triple line) sonographic endometrial pattern.

There are conflicting results regarding the correlation between endometrial thickness and pregnancy rate and proper thickness for highest pregnancy rate has not been yet found. Weissman et al.[19] reported that the pregnancy rate was decreased in cases with endometrial thickness > 14 mm which also increases the abortion risk. Rashidi et al.[20] found no significant difference in endometrial thickness between pregnant and non-pregnant women. They indicated that pregnancy occurred mostly in endometrial thickness between 9-12 mm.[20] In the present study, all pregnancies occurred in endometrial thickness of 9-14 mm. Unlike Rashidi et al.[20], the study by Momeni et al.[2] in their meta-analysis reported that endometrial thickness was higher among the pregnant women.

Table 1. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of different endometrial thicknesses and endometrial pattern alone or in combination with the endometrial thickness

Variable	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Endometrial thickness > 9.5 mm	77.50	75.45	53.45	90.22
Endometrial thickness > 7 mm	100	11.82	29.20	100
Type A endometrial pattern	87.50	35.45	33.02	88.64
Endometrial thickness > 9.5 mm and type A pattern	67.50	80.91	56.25	87.25
Endometrial thickness > 7 mm and type A pattern	100	11.82	29.20	100

PPV: Positive predictive value; NPV: Negative predictive value

In recent studies, endometrial pattern was also considered as an indicator of implantation; however, there was no consensus on the proper endometrial pattern to achieve successful pregnancy.[21] The classification of endometrial pattern varies in different studies. Similar to findings of the present study, Ma et al.[9] noted that thick endometrium and triple line endometrial pattern have significant role in pregnancy rate. Kuc et al.[22] also mentioned that triple line pattern (TLP) had significant effect on pregnancy only among the patients receiving long agonist therapy protocol. Other studies found no significant difference between different endometrial pattern and pregnancy rate.[20,23,24]

Although previous studies have shown that thin endometrium accompanies with poor pregnancy outcomes,[12,25-27] there is no accepted cut-off for endometrial thickness which could properly determine pregnancy incidence. Moreover, there are reports of pregnancy in endometrial thickness of < 6 mm and even below 4.0 mm.[16] Noyes et al.[28] observed that clinical pregnancy rate in endometrial thickness < 8.0 mm was lower than cases with endometrial thickness ≥ 9 mm. Furthermore, Al-Ghamdi et al.[4] indicated that endometrial thickness > 11 mm was acceptable for better pregnancy outcome. Kehila et al.[29] also noted that endometrial thickness > 12 mm increases the chance of successful pregnancy.

In the present study, the endometrial thickness > 9.5 mm resulted in significantly higher rate of pregnancy even higher than when considering a thickness of > 7 mm. In addition, it was observed that the combination of endometrial thickness (> 9.5 mm) and pattern (triple line) led to even higher rate of pregnancy. Chen et al.[23] reported that combination of both endometrial thickness and pattern compared to each one separately could be a better predictor of outcome of patients in IVF-ICSI cycles.

Conclusion

Thickness and pattern of endometrium both could predict pregnancy incidence. Having TLP along with endometrium thickness > 9.5 mm, the possibility of pregnancy following IVF-ICSI increases. We recommend to measure endometrial thickness and pattern among all patients receiving IVF-ICSI cycles to define the possibility rate of successful pregnancy. Moreover, if evaluations showed hypoecho pattern along with endometrial thickness < 7 mm, it is better to have cryopreservation for further cycles.

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Authors' Contribution

All authors have read and approved the manuscript. K. H., H. K. and P. K. performed the data collection, writing, critical revision and drafting of the manuscript. K. H., H. P. and P. C. contributed in the study design and performed the statistical analysis, data analysis and data interpretation.

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Conflict of Interest

Authors have no conflict of interest.

Ethical Approval

This study was approved by the Regional Medical Ethics Committee of Tabriz University of Medical Sciences under the number tbzmed.rec.95.3-5.10.

References

1. Yaman C, Mayer R. Three-dimensional ultrasound as a predictor of pregnancy in patients undergoing ART. J Turk Ger Gynecol Assoc 2012; 13(2): 128-34. DOI: 10.5152/jtgga.2012.15
2. 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; 4(3): 130-7. DOI: 10.4103/0974-1208.92287
3. McLernon DJ, Steyerberg EW, Te Velde ER, Lee

AJ, Bhattacharya S. Predicting the chances of a live birth after one or more complete cycles of in vitro fertilisation: Population based study of linked cycle data from 113 873 women. BMJ 2016; 355: i5735. DOI: 10.1136/bmj.i5735

4. 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. DOI: 10.1186/1477-7827-6-37

5. McWilliams GD, Frattarelli JL. Changes in measured endometrial thickness predict in vitro fertilization success. Fertil Steril 2007; 88(1): 74-81. DOI: 10.1016/j.fertnstert.2006.11.089

6. Amir W, Micha B, Ariel H, Liat LG, Jehoshua D, Adrian S. Predicting factors for endometrial thickness during treatment with assisted reproductive technology. Fertil Steril 2007; 87(4): 799-804. DOI: 10.1016/j.fertnstert.2006.11.002

7. Richter KS, Bugge KR, Bromer JG, Levy MJ. Relationship between endometrial thickness and embryo implantation, based on 1,294 cycles of in vitro fertilization with transfer of two blastocyst-stage embryos. Fertil Steril 2007; 87(1): 53-9. DOI: 10.1016/j.fertnstert.2006.05.064

8. Barker MA, Boehnlein LM, Kovacs P, Lindheim SR. Follicular and luteal phase endometrial thickness and echogenic pattern and pregnancy outcome in oocyte donation cycles. J Assist Reprod Genet 2009; 26(5): 243-9. DOI: 10.1007/s10815-009-9312-z

9. Ma NZ, Chen L, Dai W, Bu ZQ, Hu LL, Sun YP. Influence of endometrial thickness on treatment outcomes following in vitro fertilization/intracytoplasmic sperm injection. Reprod Biol Endocrinol 2017; 15(1): 5. DOI: 10.1186/s12958-016-0222-5

10. Gingold JA, Lee JA, Rodriguez-Purata J, Whitehouse MC, Sandler B, Grunfeld L, et al. Endometrial pattern, but not endometrial thickness, affects implantation rates in euploid embryo transfers. Fertil Steril 2015; 104(3): 620-8. DOI: 10.1016/j.fertnstert.2015.05.036

11. Zhao J, Zhang Q, Li Y. The effect of endometrial thickness and pattern measured by ultrasonography on pregnancy outcomes during IVF-ET cycles. Reprod Biol Endocrinol 2012; 10: 100. DOI: 10.1186/1477-7827-10-100

12. Aydin T, Kara M, Nurettin T. Relationship between endometrial thickness and in vitro fertilization-intracytoplasmic sperm injection outcome. Int J Fertil Steril 2013; 7(1): 29-34.

13. Laasch C, Puscheck E. Cumulative embryo score, not endometrial thickness, is best for pregnancy prediction in IVF. J Assist Reprod Genet 2004; 21(2): 47-50. DOI: 10.1023/B:JARG.0000025937.43936.73

14. Garcia-Velasco JA, Isaza V, Caligara C, Pellicer A, Remohi J, Simon C. Factors that determine discordant outcome from shared oocytes. Fertil Steril 2003; 80(1): 54-60. DOI: 10.1016/S0015-0282(03)00545-4

15. Dietterich C, Check JH, Choe JK, Nazari A, Lurie D. Increased endometrial thickness on the day of human chorionic gonadotropin injection does not adversely affect pregnancy or implantation rates following in vitro fertilization-embryo transfer. Fertil Steril 2002; 77(4): 781-6. DOI: 10.1016/S0015-0282(01)03276-9

16. Sundstrom P. Establishment of a successful pregnancy following in-vitro fertilization with an endometrial thickness of no more than 4 mm. Hum Reprod 1998; 13(6): 1550-2.

17. Revel A. Defective endometrial receptivity. Fertil Steril 2012; 97(5): 1028-32. DOI: 10.1016/j.fertnstert.2012.03.039

18. Gonen Y, Casper RF, Jacobson W, Blankier J. Endometrial thickness and growth during ovarian stimulation: a possible predictor of implantation in in vitro fertilization. Fertil Steril 1989; 52(3): 446-50. DOI: DoI: 10.1016/S0015-0282(16)60916-0

19. Weissman A, Gotlieb L, Casper RF. The detrimental effect of increased endometrial thickness on implantation and pregnancy rates and outcome in an in vitro fertilization program. Fertil Steril 1999; 71(1): 147-9.

20. Rashidi BH, Sadeghi M, Jafarabadi M, Tehrani Nejad ES. 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): 179-84. DOI: 10.1016/j.ejogrb.2004.08.016

21. 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): 101-4. DOI: 0172002/AIM.008

22. Kuc P, Kuczynska A, Topczewska M, Tadejko P, Kuczynski W. The dynamics of endometrial growth and the triple layer appearance in three different controlled ovarian hyperstimulation protocols and their influence on IVF outcomes. Gynecol Endocrinol 2011; 27(11): 867-73. DOI:10.3109/09513590.2010.540602

23. Chen SL, Wu FR, Luo C, Chen X, Shi XY, Zheng HY, et al. Combined analysis of endometrial thickness and pattern in predicting outcome of in vitro fertilization and embryo transfer: a retrospective cohort study. Reprod Biol Endocrinol 2010; 8: 30. DOI: 10.1186/1477-7827-8-30

24. Merce LT, Barco MJ, Bau S, Troyano J. Are endometrial parameters by three-dimensional ultrasound and power Doppler angiography related to in vitro fertilization/embryo transfer outcome? Fertil Steril 2008; 89(1): 111-7. DOI: 10.1016/j.fertnstert.2007.02.029

25. Habibzadeh V, Nematolahi Mahani SN, Kamyab H. The correlation of factors affecting the endometrial

thickness with pregnancy outcome in the IUI cycles. Iran J Reprod Med 2011; 9(1): 41-6.

26. Bu Z, Sun Y. The impact of endometrial thickness on the day of human chorionic gonadotrophin (hCG) administration on ongoing pregnancy rate in patients with different ovarian response. PLoS One 2015; 10(12): e0145703. DOI: 10.1371/journal.pone.0145703

27. 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. DOI: 10.1186/1477-7827-12-96

28. Noyes N, Hampton BS, Berkeley A, Licciardi F, Grifo J, Krey L. Factors useful in predicting the success of oocyte donation: a 3-year retrospective analysis. Fertil Steril 2001; 76(1): 92-7.

29. Kehila M, Kebaili S, Bougmiza I, Meddeb S, Boughizane S, Khairi H, et al. Endometrial thickness in in vitro fertilization. A study of 414 cases. Tunis Med 2010; 88(12): 928-32. [In French].