The Relationship Between Endometrial Thickness and Endometrial Pattern With Pregnancy Rate Based on Positive Serum Beta-Human Chorionic Gonadotropin

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Abstract

Objectives: Infertility is defined as the lack of pregnancy after one year of sexual contact without using any contraception. The aim of this study was to investigate the association between endometrial thickness (ET) and endometrial pattern with beta-human chorionic gonadotropin (B-HCG) test in women undergoing the induction of ovulation who referred to the infertility clinic of Ali ibn-e Abitalib hospital in Zahedan.

Materials and Methods: This cross-sectional study was conducted at Ali ibn-e Abitaleb hospital in Zahedan (Iran) in 2017. The ET and endometrial pattern were estimated using transvaginal sonography and the pregnancy rate was determined based on B-HCG test. Finally, the data were analyzed by SPSS using the Chi-square test and independent t-test.

Results: A total of 200 individuals with a mean age of 29.6 ± 5.6 years were evaluated in this study. The negative or positive B-HCG distribution was significantly different in terms of the endometrial pattern (P=0.001) so that 35.3% of women had B-HCG positive cases in the three-line pattern of ET while in the homogenous pattern, 3.3% had B-HCG positive cases. In addition, the pregnancy rate in women with ET greater than 7 mm was significantly higher compared to those women with ET less than 7 mm thickness (35.1% vs. 12.8%, P<0.001).

Conclusions: Overall, the results of this study showed a significant correlation between the endometrial pattern and ET and pregnancy rate based on positive B-HCG test.

Keywords: Endometrial thickness, endometrial pattern, Serum BHCG, Induction of ovulation

Introduction

Infertility is considered as the lack of pregnancy after 12 months (or more) of unprotected intercourse without using any contraception (1). In addition, infertility is one of the most common problems of societies, and according to a large systematic analysis published in 2012, approximately 45-52.6 million couples (on average 48.5 million couples) suffer from this problem (2).

Female factors are the most common causes of infertility, among which, ovulatory disorders are the most prevalent reasons for female infertility. Induction ovulation is regarded as the main treatment for ovulatory disorders, and in cases of unexplained infertility, as well as the poor male and cervical factors, induction ovulation is associated with intrauterine insemination (IUI) therapy is used that increases the number of oocytes and sperm motility and thus eliminate cervical factor (3).

IUI is a procedure in which processed and concentrated motile sperms are directly placed into the uterine cavity.

The clinical use of IUI is based on the hypothesis that placing the excessive numbers of sperm high in the reproductive tract enhances the likelihood of conception.

The minimum requirements for performing the procedure are ovulation in the IUI cycle, the patency of at least one fallopian tube, insemination with an adequate number of motile sperm, and the absence of documented or suspected active cervical, intrauterine, or pelvic infection (4). Shokoohi et al investigated the effect of onion juice on male factor infertility and pregnancy rate by IUI (5).

Endometrial thickness (ET) and endometrial pattern contribute to the success of the assisted reproductive technology. Although endometrial evaluation is a standard procedure during diagnostic evaluation and infertility treatment, the clinical significance of the difference in thickness and the appearance of the endometrium is still discussed and several studies show a meaningful relationship between the amount of pregnancy and the thickness of the endometrium while other studies reject the presence of such a connection (6-9).

Based on the results of a large-scale study on 12 285 couples in 30 provinces in 2008, the prevalence of infertility was reported 8% in Iran (10). Further, the findings of another study conducted in Iran showed the prevalence of infertility was 2.5% and the national study

estimated the prevalence of primary infertility by 1.6%. Furthermore, in another similar study, primary and secondary infertility were estimated to be 1.7% and 10.5%, respectively. Nowadays, many infertile couples (40-50%) have the chance of pregnancy with the advent of science and the use of modern methods of infertility treatment (10).

The present study aimed to evaluate the relationship between thickness and endometrial pattern with B-HCG test in women who underwent induction ovulation referring to the Obstetrics and Gynecology Clinic of Ali ibn-e Abitaleb hospital in Zahedan (Iran).

Materials and Methods

This descriptive-analytical study was conducted at Ali ibn-e Abitaleb Hospital in Zahedan during 2017 and investigated 200 patients with infertility who referred to the Obstetrics and Gynecology Clinic of Ali ibn-e Abitaleb hospital in Zahedan. The inclusion criteria included all patients with ovulatory dysfunction, ages 35-18, and at least one year of marriage age, and the exclusion criteria were endometrial polyps, uterine anomalies, and reluctance to participate in the study.

In all patients, measuring the thickness of the endometrium and examining its pattern was performed after 15 minutes of rest and complete bladder emptying. All sonography was performed by an experienced sonographer with a single ultrasound device and the endometrial pattern was characterized by transvaginal ultrasonography as homogeneous or triple-line. After measuring the thickness of the endometrium and determining its pattern, serum letrozole 5 mg (based on infertility literature) was prescribed from day 3 to day 7 of the menstrual cycle for each patient, and after 2 to 3 weeks, the serum B-HCG was measured to determine the pregnancy.

Data were analyzed by SPSS software, version 22 using the chi-square test and independent *t* test.

Data Collection

To describe the data, descriptive statistics including the central indexes and distributions and distances, as well as statistical charts were used. Eventually, the chi-square test and independent t-test were applied for data analysis.

Results

A number of 200 individuals with a mean age of 29.6 ± 5.6 years were investigated in the current study. Totally, 69.8% of the patients had triple-line endometrial pattern while 30.2% of them had a homogeneous pattern. B-HCG test was positive in 25.6% of women.

The chi-square test was used to analyze the data (Table 1). The results showed that B-HCG negative or positive distribution significantly differed in terms of the endometrial pattern (*P*=0.001) so that in triple-line endometrium pattern, about 35.3% had positive

B-HCGs while in the homogeneous pattern, nearly 3.3% were positive BHCG. To report the correlation of endometrial pattern with positive or negative B-HCG, the phi coefficient was used, which was estimated as 0.33. In addition, the chance for positive B-HCG in those having triple-line endometrial pattern was 15 times as high as those having the homogeneous endometrium. Based on the results of independent t-test, the mean ET demonstrated no significant difference in both groups with positive and negative B-HCG (*P* = 0.73), the details of which are provided in Table 2.

In order to report the correlation of endometrial pattern with positive or negative B-HCG, the phi coefficient was used which was 0.33. In addition, the positive B-HCG chance for triple-line endometrium was 15 times as high as those patients with the homogeneous endometrium (Figure 1).

One woman with heterogeneous endometrium was discarded from the analysis.

Discussion

Infertility in a couple is regarded as the inability to achieve conception despite one year of frequent unprotected intercourse, which is one of the most frequent problems of human societies (1,2). According to World Health Organization, between 60 and 80 million couples around the world suffer from this problem and female and male factor infertility were reported in 37% and 80% of infertile couples in developed countries and both male and female factor infertility were estimated as 35%. The remaining couples had unexplained infertility.

Based on the results of the study by Behnoud et al (11), the most common identifiable female factors, which accounted for 81% of female infertility included ovulatory disorders (25%), endometriosis (15%), pelvic adhesions (12%), tubal blockage (11%), other tubal abnormalities

Table 1. Distribution of Positive and Negative B-HCG Posology by Endometrial Pattern in Women Under Induction Ovulation

	B-HCG		Total
	Negative	**Positive**	
Endometrial pattern			
Triple-line, No. (%)	90 (64.7)	49 (35.3)	139 (69.8%)
Homogeneous, No. (%)	58 (96.7)	2 (3.3)	60 (30.2%)
Total, No. (%)	148 (74.5)	51 (25.5)	199 (100%)

B-HCG: Beta-human chorionic gonadotropin.

Table 2. Comparison of Endometrial Thickness in Women With B-HCG Positive and Negative

BHCG	No. (%)	Mean ± SD	*P* Value
Negative	148 (74.3%)	7.3 ± 1.5	0.73
Positive	51 (25.6%)	8.5 ± 1.4	

B-HCG: Beta-human chorionic gonadotropin; SD: standard deviation.
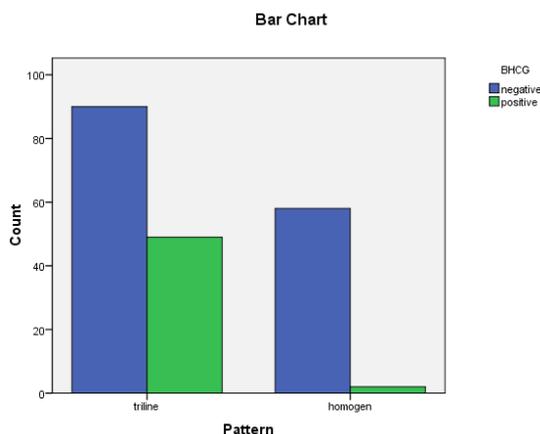
Figure 1. The correlation of endometrial pattern with positive or negative B-HCG.

(11%), and hyperprolactinoma (7%).

The aim of the current study was to determine the relationship between ET and endometrial pattern with B-HCG positive in women who underwent induction ovulation referring to infertility clinic of Ali ibn-e Abitaleb hospital in Zahedan. ET and endometrial pattern contributed to the success of assisted reproductive technologies. Although endometrial evaluation with ultrasound is a standard procedure for the evaluation of diagnosis and treatment of infertile women, the clinical importance of the difference between ET and endometrial pattern is controversial. Several studies showed a significant relationship between the pregnancy rate and ET while other studies denied such an association.

The results of our study revealed that 69.8% of pregnancies were based on a triple-line endometrial pattern while 30.2% included a homogeneous pattern (Table 1). Further, B-HCG test was positive in 25.6% of the patients and the rate of positive B-HCG was significantly higher in patients with a triple-line endometrial pattern than those with a homogeneous pattern.

In a study by Zhao et al in China in 1933, IVF-treated women had more pregnancy in the triple-lined pattern than in the homogeneous one (7). Contrary to the results of our study, in the study by Hosseini Rashidi et al on 150 infertile women, the incidence of pregnancy following IVF/ICSI was 20%, but there was no relationship between the endometrial pattern and pregnancy rate (8). Similarly, in another study by Zhao et al, the highest clinical pregnancy rate was observed in patients with a triple-line pattern (9). However, the difference in the results of various studies in this area can be due to different design studies and the fact that the results of ultrasound evaluation are completely dependent on a person. On the other hand, the exact mechanism of the effect of endometrial pattern on pregnancy rate is not known and thus requires further investigation.

In this study, the mean ET was not significantly different between the two groups with positive and negative B-HCG

($P = 0.73$). However, by categorizing the patients based on the thickness of the endometrium into two groups of <7 mm and >7 mm, the results of the chi-square showed that the gestational age was significantly greater in ET group >7 mm in comparison with patients with ET<7 mm (35.1% vs. 12.8%, $P < 0.001$). Zhao also declared that the thickness of the endometrium could be considered as an independent factor in predicting the pregnancy rate and the highest pregnancy rate was in the thickness between 7-14 mm (7). Similarly, Esmailzadeh et al found that the mean ET in the pregnant women group was significantly higher than non-pregnant women (5). In contrast to the results of our study, Hosseini Rashidi in their study demonstrated that the mean thickness of endometrium in pregnant women was not significantly different between pregnant women (8). These contradictions in the results of different studies in this area may be attributed to the time of measuring the ET. According to the report by Zhao et al, the endometrium of pregnant women was not comparable with that of the pregnant women and endometrium was thinner on the third day while it was thicker on the day of HCG prescription (9-11).

Study Limitations
There was no specific limitation on the implementation of this study.

Conclusions
In general, the results of this study confirmed that the fertility rate was significantly higher in women with an endometrial triple-line pattern and those with an ET greater than 7 mm compared to women with a homogeneous pattern and ET less than 7 mm that is practical for infertility treatment.

Conflict of Interests
Authors declare that they have no conflict of interests.

Ethical Issues
Written informed consent was obtained from all participants in this study and this plan was approved by the Ethics Committee of Zahedan University of Medical Sciences under the ethical code of IR.ZAUMS. REC.1395.96.

References

1. Definitions of infertility and recurrent pregnancy loss: a committee opinion. Fertil Steril. 2013;99(1):63. doi:10.1016/j.fertnstert.2012.09.023

2. Mascarenhas MN, Flaxman SR, Boerma T, Vanderpoel S, Stevens GA. National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys. PLoS Med. 2012;9(12):e1001356. doi:10.1371/journal.pmed.1001356

3. Fouda UM, Sayed AM. Extended letrozole regimen versus clomiphene citrate for superovulation in patients with unexplained infertility undergoing intrauterine insemination: a randomized controlled trial. Reprod Biol Endocrinol. 2011;9:84. doi:10.1186/1477-7827-9-84

4. Esmailzadeh S, Faramarzi M. Endometrial thickness and pregnancy outcome after intrauterine insemination. Fertil Steril. 2007;88(2):432-437. doi:10.1016/j.fertnstert.2006.12.010

5. Shokoohi M, Olad-Saheb-Madarek E, Khaki A, et al. Investigating the effects of onion juice on male fertility factors and pregnancy rate after testicular torsion/detorsion by intrauterine insemination method. Int J Womens Health Reprod Sci. 2018;6(4):499-505. doi:10.15296/ijwhr.2018.82

6. 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;2(4):323-335. doi:10.1093/humupd/2.4.323

7. 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

8. Hosseini Rashidi B, 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):179-184. doi:10.1016/j.ejogrb.2004.08.016

9. 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;29(3):291-298. doi:10.1016/j.rbmo.2014.05.011

10. Behnoud N, Bahrami R, Kordafshari G, Farzaneh F, Mohammadi Kenari H. Management of Early Menopause Using Traditional Persian Medicine: A Case Report. Int J Womens Health Reprod Sci. 2019;7(2):231-236. doi:10.15296/ijwhr.2019.39

11. Behnoud N, Farzaneh F, Ershadi S. The effect of clomiphene citrate versus letrozole on pregnancyrate in women with polycystic ovary syndrome: a randomized clinical trial. Crescent Journal of Medical and Biological Sciences. 2019;6(3):335-340.