

# Evaluating Endometrial Thickness and Vascular Ultrasound Pattern and Pregnancy Outcomes in Intrauterine Insemination Cycle

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## Abstract

The current study aims to investigate whether endometrial thickness and pattern, and blood flow in color Doppler of sonography on the day of administration is a predictor of intrauterine insemination (IUI) success. The study was designed as a cross-sectional prospective clinical study with one-hundred women undergoing an IUI cycle. Interventions of the study include endometrial thickness and pattern and color Doppler flow on the day of administration and cycle parameters were compared between pregnant and non-pregnant patients. Main outcome measures are endometrial thickness and patterns and blood flow in color Doppler. The results showed that the overall pregnancy rate was 38%, which mean that endometrial blood flow on the day of administration was significantly greater in cycles, pregnancy achieved, but endometrial thickness and pattern of sonography were found to have no predictive value on endometrial receptivity. In multi-variant analysis, the following variable affected the pregnancy rate: the women's age, duration of infertility, type, number of IUI cycle, the number of ampules to stimulate dominant follicle, sperm count. In our study, this variability was found to have no predictive value on the outcome of IUI but endometrial flow in color Doppler was positively associated pregnancy outcome.

**Keywords:** Endometrial Thickness, Polycystic Ovarian Syndrome, Vascular Ultrasound Insemination Cycle

## 1. Introduction

Infertility means not getting pregnant while having unprotected intercourse for one year. Infertility occurs in approximately 10-15% of couples and forms an important problem of the clinical practice of physicians account<sup>1,2</sup>.

There are several methods for infertility treatment, the oldest of which IUI and artificial insemination; most important indications of IUI include male infertility, cervical factor, and difficulties which impede transition of the sperm towards oocyte. Implantation is such an important step in fertility that its defect can be a major cause of treatment failure in IUI or COH cycles<sup>3,4</sup>. The implementation is so central that can function as a

distinguishing factor between reproductive and failed cycles.

Several ultrasound parameters, such as uterine endometrial thickness and blood flow, have been studied to assess the acceptance of the uterus. Some studies have foregrounded blood content as a significant criterion of uterus acceptance; other studies, also, have foregrounded uterine blood and endometrial flow as factors influential in enhancing the possibility of pregnancy during IVF cycles<sup>5</sup>. Though different studies have focused on ultrasound pattern and endometrial thickness on the day of hGG injection, there is no consensus about the effectiveness of these factors during IUI cycles<sup>6,7</sup>. On the other hand, no study has, so far, discussed different characteristics of

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the endometrial during IUI or IVF cycles simultaneously; therefore, this study aims, primarily, at evaluating endometrium general characteristics such as endometrial thickness, endometrial vascular rate, ultrasound picture, and flow rate on the day of the injection of in IUI cycles in order to, in case of endometrial difficulty, either cancel the cycle or do intervention in a more appropriate time.

## 2. Materials and Methods

This was a cross-sectional prospective study in which patients were IUI candidate patients were chosen in the simple randomize sampling form. This study included 100 patients, aged between 21-38 years, who referred to Shahid Akbarabadi Infertility Center during September 2013 to August 2014; the stimulation protocol was selected individually based on factors like age, diagnosis, a history of infertility, and medical condition<sup>8</sup>. When the diameter of the largest follicle in the follicular phase was less than 10, the patient was exposed to COH through the administration of gonadotropin with FSH or without hMG<sup>13,14</sup>. The initial dose of gonadotropin was between 150-450 iu and it varied based on FSH level, antral follicles, and the patient's age. 10000 units of hGG were prescribed when there were two less than 18 mms follicles; on the day of administration, patients were exposed to trans-vaginal ultrasound and Doppler to assess endometrial thickness, endometrial and flow pattern of blood vessels; 36-48 hours after injection, IUI was performed. Then their blood samples were taken at day 14<sup>th</sup> after IUI and a more than 15 headline was considered positive. Clinical pregnancy was determined based on detection of fetal heart rate in the sixth week of pregnancy by trans-vaginal ultrasound and the subjects were classified in two pregnant and non-pregnant individuals; the two groups were compared based on various parameters such as age, duration of infertility, stimulation duration, number of injections, endometrial thickness, endometrial vascular flow pattern, and ultrasound. Endometrial thickness, vascular flow, and its pattern were evaluated 11-12 hours after administration by trans-vaginal ultrasound and Doppler 15 minutes after patients had emptied their bladders and rested (ultrasound with Siemens G50, probes 4/9 MHz). All patients had an ultrasound between 9-11 a.m. by a fixed person.

Patients were divided into three categories in regard with endometrial thickness:

- $ET \geq 7$
- $7 < ET < 14$
- $ET \leq 14$

Endometrial ultrasound pattern was also divided into three sections:

- Triple-line including central hyper echo lines which were surrounded by two hypo-echo layers.
- Average ISO echo area and central echogenic line surrounded by approximately unknown boundaries
- Hyper-echoic endometrial and homogeny

Blood flow was, also, described in following three ways:

- No flow
- Low blood flow
- Significant vascular flow

Inclusion criteria:

- The content of the patients
- Candidate IUI (unexplained infertility, cervical problems (cervical mucus or due to previous problems of the cervix), PCO, male factor)
- 21-38 years of age

Exclusion criteria:

- Endometrial polyps
- Uterine anomalies
- Any uterine changes which disorients endometrial view

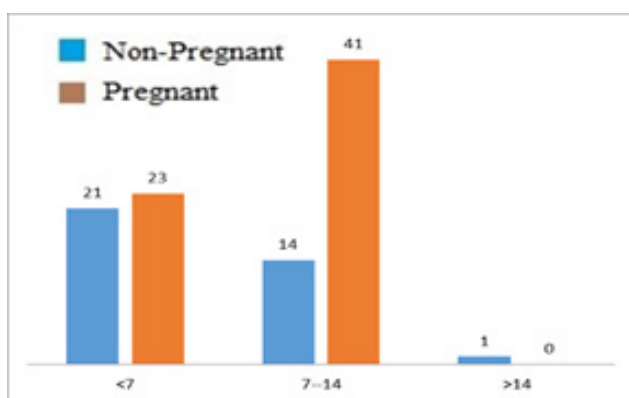
## 3. Results

This study included 100 women with infertility difficulties underwent IUI; 83 patients (83%) were less than 35 years and 17 patients (17%) were over 35 years old. 75 patients with primary infertility and 25 patients due to secondary causes had been admitted to the center. Patients were also evaluated in terms of causes of infertility and according to the results, 54 patients (54%) for male reasons, 42 cases (42%) of polycystic ovary, 3 patients (3%) of above the average age, and 1 case of unexplained cause was reported.

Blood samples were collected to evaluate the  $\beta$ criteria and values above 15 were considered as pregnant; serum samples from 36 patients with  $\beta$ criteria was positive and these patients were considered pregnant. An ultrasound

was done on the patients during the sixth week and in the case of presence of FHR, they were diagnosed with clinical pregnancy. Accordingly, fetal heart rate was confirmed in all 36 cases and a definite diagnosis of pregnancy was confirmed.

The average duration of infertility period was  $1/6 \pm 3/7$  years in pregnant women and  $2/9 \pm 4/2$  in non-pregnant women; independent t-test showed no significant difference between them ( $p = 0/310$ ). In pregnant women, 28 subjects had less than 6 and 7 subjects more than 6 ampoule injection to treat their infertility; in the group of non-pregnant women 55 patients received less than 6 while 9 cases more than 6 ampoule injections. Collected data were analyzed through Chi-square test and it showed no significant difference between two groups ( $p = 0/240$ ) (Figure 1).

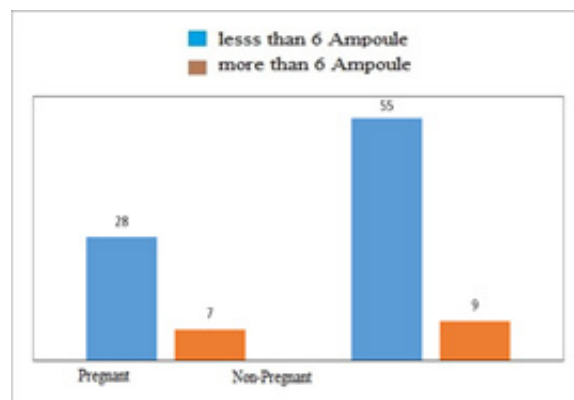


**Figure 1.** Number of shots taken (blue: less than 6; red: more than 6 shots).

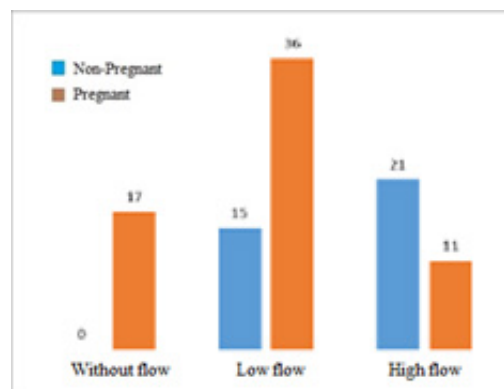
Base FSH values were  $3/5 \pm 6/3$  in pregnant women, and  $5/5 \pm 6/1$  in non-pregnant women. The analysis of data through independent t-test showed no significant differences in basal FSH serum between two groups ( $p = 0/176$ ). 6 patients (6/16%) in the pregnant group and 11 (2/17%) cases in the non-pregnant group were older than 35 years. Data analysis through Chi-square test showed no significant difference between two groups ( $p = 0/614$ ), (Figure 2 and Figure 3).

Finally, two groups of pregnant and non-pregnant patients were compared in regard to endometrial thickness, endometrial blood flow, and pattern of endometrial ultrasound. Endometrial thickness was defined in three following ways; in the group of pregnant women, 21 (58/3%) subjects with less than 7 endometrial

thickness, 14 (38/9%) cases with endometrial thickness between 7 and 14, and one case of more than 14 thickness; in the non-pregnant group, and 23 patients (35/9%) with endometrial thickness of less than 7 and 41 patients (64/1%) had a thickness between 7-14. Data analysis using Chi-square test showed significant differences in endometrial thickness between two groups ( $p = 0/029$ ).



**Figure 2.** Endometrial thickness in pregnant and non-pregnant patients (blue: pregnant; red: non-pregnant).



**Figure 3.** Vascular endometrium flow in pregnant and non-pregnant patients.

Endometrial blood flow was determined by Doppler ultrasonography. In this regard, in the group of pregnant women, 21 patients (58/3%) with significant blood flow and 15 patients (41/7%) with the mild blood flow were diagnosed; in non-pregnant group of women, 17 patients (26/2%) cases without flow, 36 patients (56/2%) with mild flow, and 11 patients (17/2%) with significant flow were diagnosed. Data analysis, through the Chi-square test, showed a significant difference between two groups in terms of endometrial blood flow ( $p = 0/00$ ).

The endometrial ultrasound pattern was briefly

expressed as t A, B, and C. In pregnant women, 20 cases (55/5%) were represented as pattern A, 13 cases (36/1%) as pattern B, and 3 cases (8/4%) as pattern C. Data analysis, through Chi-square test, also showed no significant difference between groups in the pattern of endometrial ultrasound ( $p=0/198$ ).

## 4. Discussion

Based on the results of the present study, endometrial flow in women who became pregnant through IUI cycles is significantly different from that of those women who did not get pregnant. The women who experienced a more successful cycle had higher endometrial vascular flow compared to non-pregnant women; however, endometrial thickness was higher in most non-pregnant women than pregnant women; the endometrial thickness of non-pregnant women were between 14-7 mm, while it was less than 7 mm in pregnant women; the endometrial ultrasound pattern showed no significant difference between two groups

Based on the results of the present study, endometrial thickness lacks the potential of predicting the success of IUI cycles. Based on the results of Yaman and his colleague's study, endometrial volume measurements by three-dimensional ultrasound can predict pregnancy in ART cycles<sup>9</sup>. Tsai and his colleagues found out that women, whose ultrasound showed triple-line patterns, became pregnant more frequently than women without this pattern<sup>10</sup>. Kovacs and his colleagues stated that an at least 10 mm increase in endometrial thickness is directly associated with an increased rate of pregnancy<sup>11</sup>. However, not all studies have delivered homogenous results and some does not yield any significant relationship between endometrial thickness and pregnancy outcome<sup>12-15</sup>. Weissman and his colleagues stated that implantation and pregnancy in women who had  $\leq 14$  mm endometrial thickness on the day of injection<sup>16</sup>, had a lower pregnancy rate, while Dietterich and his colleagues did not find out any harmful effect caused by endometrial thickening (mm  $14 <$ ) on the amount of implantation, pregnancy, and the abortion<sup>17</sup>. The results of Esmaeilzade and his colleagues' study<sup>2</sup>, which was consistent with ours, showed a significant difference between the mean of endometrial thickness and pregnancy outcome in IUI cycles.

Reuter and his colleagues concluded that endometrial thickness of at least 8 mm and a higher number of follicles

(up to three) is associated with higher rates of pregnancy<sup>18</sup>. Based on the results of Tomlinson and colleagues' study, the endometrial thickness is one of the main variables for predicting pregnancy outcome<sup>19</sup>.

Hock and his colleagues<sup>20</sup> studied endometrium using ultrasound; they found that a homogeneous pattern is on the day of injection is associated with decreased pregnancy rates, but this is not applicable to the triple-line pattern. In another study which was conducted by Habibzadeh and his colleagues, the results showed that there is no association between age, number of follicles, and gonadotropin ampoules with endometrial thickness; however, the chances of pregnancy are higher in endometrial thickness between 6-10 mm regardless of age more<sup>4</sup>. Based on the results of Kamath and his colleagues' study, though the rate of pregnancy in endometrial thickness more than 6 mm presented higher chances of pregnancy, this difference was not significant<sup>21</sup>.

Based on the present study, older age is not associated with adverse pregnancy outcomes; these findings are not consistent with the results of Esmaeilzade's research which examined the endometrial thickness and pregnancy outcome and showed that age was negatively associated with pregnancy outcome in women who are undergoing IUI<sup>2</sup>. Ghosh and his colleagues' study showed the possibility of pregnancy in women over 30 years as half of women less than 30 years<sup>22</sup>. But another study which was conducted by Iberico and colleagues on 1010 IUI cycles, concluded that age is not a significant predictor of pregnancy outcome<sup>23</sup>. This result is consistent with finding of the present study and was, also, approved by Geyter and his colleagues<sup>24-26</sup>. A Low sample size of patients included here can be considered as one of the limitations of this study; moreover, the quality of the sperms must have been evaluated before.

## 5. Conclusion

The use of ultrasound is an applicable and effective way of evaluating of endometrial and uterine blood flow; generally, it seems that vascular endometrium flow can have the potential of predicting the results of IUI cycles. According to this study, there is no correlation between the increase in endometrial thickness and pregnancy rate; however, wider researches are needed to achieve more precise and applicable results.



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