INTRODUCTION

According to the European Society for Human Reproduction and Embryology, infertility is described as the inability to conceive after one year of marriage or within two years, and it affects 10-15 percent of couples.\(^1\) Primary infertility is defined as an infertile female who has never conceived, and secondary infertility is a female who has conceived before. Infertility that cannot be explained by a medical condition is known as unexplained infertility. This condition is termed so when the couple is unable to conceive a child despite making repeated attempts to do so for a period of at least one year, or for a period of at least six months in women who are 35 or older.\(^2\) 10–25% of the infertile females are diagnosed with unexplained infertility since it has no definitive cause for infertility.\(^3\) A practitioner will make a diagnosis of unexplained infertility if the findings of the assessment of conventional infertility are normal.\(^4\) The following list, in descending order of prevalence, details the most prevalent identified causes of female infertility:

- Ovulatory disorders - 25%
- Endometriosis - 15%
- Pelvic adhesions - 12%
- Tubal blockage - 11%
- Other tubal or uterine abnormalities - 11%
- Hyperprolactinemia - 7%

The factors that might lead to a woman's inability to conceive a child can be broken down into seven categories: anatomic, genetic, endocrinological, microbiological, immunological, and environmental. The uterine and ovarian perfusion on color doppler examination, which is related to the pathophysiology of infertility, has, however, received little research.\(^3\) Since an adequate blood supply to the endometrium is an essential component of proper implantation,
transvaginal sonographic evaluations using both pulsed and color Doppler have been utilized to show this ideal blood supply. Uterine and ovarian perfusion also varies in response to the hormonal changes that occur throughout the menstrual cycle, which may be easily observed via transvaginal color Doppler examination and can be used to its advantage in determining the reason for infertility. This is particularly useful in situations when the cause of infertility cannot be explained. It has been discovered that fertile women have an increase in uterine and spiral artery perfusion during the luteal phase, which happens to coincide with the window of implantation. Endometrial receptivity is also regulated by uterine perfusion. It has been demonstrated in several studies that a rise in the impedance of the uterine artery during the mid-luteal phase is associated with a decrease in uterine receptivity. This abnormal uterine perfusion is a potential cause of infertility, particularly in couples who have been diagnosed with unexplained infertility. The endometrium transitions from trilaminar appearance to thicker and more homogenous appearance in the duration of mid-luteal phase. During this period, the uterine perfusion is increased, and as a result, the impedance of the uterine artery is decreased. This results in an increase in the receptivity of endometrium.

Transvaginal sonography combined with color Doppler evaluation, thus serves as an important tool for evaluation of female infertility since it is a relatively inexpensive, safe, radiation free, non-invasive investigation, easy to use and easily repeatable approach to assess the uterine perfusion and changes in female reproductive physiology. There are three different ways that endometrial morphology may be described: trilaminar, homogeneous, and heterogeneous. A trilaminar endometrium is a sonological appearance that signifies a hypoechoic middle functional layer of endometrium, peripheral hyperechoic basal layers and a central echogenic line. This pattern of appearance can be seen during the late proliferative phase or follicular phase of the menstrual cycle, ideally from five to six days before the day of ovulation and continues until the day of ovulation. During this time, a woman is most likely to become pregnant.

This trilaminar appearance of endometrium during the time of the injection like hCG or GnRH agonist that trigger the ovulation cycle, has been observed to back up the higher rates of pregnancy in IVF cohorts. Understanding the sonological pattern of endometrium appearance during different phases of menstrual cycle is essential for monitoring during IUI, or IVF cycles. There is limited literature about the usefulness of the Ultrasononography and Color Doppler in female infertility. The present study compared the Ultrasononography and Color Doppler for assessment in female infertility.

**Aim of the Study**
- Role of Endometrial Color Doppler evaluation in female infertility.

**Objective of the Study**
To Assess the Endometrial Thickness, physiological variations and vasculature using color Doppler on transvaginal ultrasound.

**MATERIALS AND METHODS**
This prospective, observational study was conducted in our institution over a period of 18 months on sixty patients following approval from Institutional Ethic Committee and written informed consent using the following criteria strictly:

**Inclusion Criteria**
- Infertile females of 18-37 years of age.

**Exclusion Criteria**
- Structural abnormalities of uterus
- Endocrinological systemic disorders
- Male partner infertility

Doppler assessment and TVS were done on SIEMENS ACUSON S2000 with MC 9-4Hz Transvaginal probe. Scan was done on the first day of menstruation for a baseline evaluation to assess the basic anatomy & sizes of the uterus, endometrium, both the ovaries and adnexa. Then the scans were done in periovulatory phase and mid-luteal phase during the treatment to assess the following:

- Endometrial thickness, endometrial type and grading of endometrial vascularity.
- Endometrial typing was assessed based upon Sher et al classification in 1991 that is:
  - Non-multilayered - homogeneous hyperechogenic or iso-echogenic endometrium compared with the myometrium
  - Multilayered – Trilaminar appearance = outer peripheral layer of denser echogenicity and a central sonolucent area.
- Endometrial perfusion was assessed based on the Modified Applebaum Uterine Scoring System:
  - ZONE 1- Myometrium surrounding the Endometrium
  - ZONE 2- Hyperechoic endometrial line
  - ZONE 3- Internal endometrial hyperechoic zone
  - ZONE 4- Endometrial Cavity

The treatment given to the patients before IVF was: Folic acid tablets, Ecosprin, Estradiol, Levonordestrel Ethinyloestradiol tablets, Tab. Sildenafil and Vitamin K2.

Treatment after IVF given was: Tab. Progesterone, Inj. hCG twice a week, Inj. Enoxaparin, Inj. Filgrastim once a week and Inj. Progesterone.
RESULTS

Table 1: Study population according to Age

The population that was being studied had a mean age of 28.77±4.95 years (ranging from 20.00 to 37.00 years).

Table 2: Study population according to endometrial size

<table>
<thead>
<tr>
<th>Endometrium</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>4.57</td>
<td>1.14</td>
<td>2.80</td>
<td>7.00</td>
</tr>
<tr>
<td>Proliferative</td>
<td>6.69</td>
<td>1.05</td>
<td>3.80</td>
<td>8.60</td>
</tr>
<tr>
<td>Secretory</td>
<td>7.86</td>
<td>1.38</td>
<td>4.20</td>
<td>10.60</td>
</tr>
</tbody>
</table>

The mean Endometrium at Baseline, Proliferative and Secretory phase was 4.57±1.14, 6.69±1.05 and 7.86±1.38 respectively.

Table 3: Distribution of study population according to endometrial perfusion grading associated with endometrial typing and their treatment outcomes

<table>
<thead>
<tr>
<th>Endometrial Blood flow</th>
<th>No of cases</th>
<th>Type of Endometrium</th>
<th>T/T</th>
<th>No. of Pregnant cases</th>
<th>No. of Non- Pregnant cases</th>
<th>Pregnancy rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zone 1</td>
<td>19</td>
<td>Non-multilayered</td>
<td>13</td>
<td>4</td>
<td>9</td>
<td>30.8%</td>
</tr>
<tr>
<td>Zone 2</td>
<td>22</td>
<td>Non-multilayered</td>
<td>11</td>
<td>5</td>
<td>6</td>
<td>45.5%</td>
</tr>
<tr>
<td>Zone 3</td>
<td>14</td>
<td>Non-multilayered</td>
<td>8</td>
<td>8</td>
<td>0</td>
<td>100.0%</td>
</tr>
<tr>
<td>Zone 4</td>
<td>5</td>
<td>Multilayered</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>100.0%</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.001*</td>
</tr>
</tbody>
</table>

100% pregnancy rates were seen in women with Zone 3 and 4 vascularity, respectively.

Table 4: Study population according to endometrial type

<table>
<thead>
<tr>
<th>Treatment taken</th>
<th>No of cases</th>
<th>Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multilayered</td>
<td>16</td>
<td>100.0%</td>
</tr>
<tr>
<td>Non-Multilayered</td>
<td>20</td>
<td>25.0%</td>
</tr>
<tr>
<td>p-value</td>
<td>0.001*</td>
<td></td>
</tr>
</tbody>
</table>

Pregnancy rate was significantly higher among multilayered group.

Figure 1: The mean Endometrium at Baseline, Proliferative and Secretory phase was 4.57±1.14, 6.69±1.05 and 7.86±1.38 respectively.

Figure 2: Bar graph depicting endometrial appearance, number of patients who took treatment and their pregnancy outcomes in respective Zones of vascularity. 100% pregnancy rates were seen in women with Zone 3 and 4 vascularity, respectively.

Figure 3: Pregnancy rate was significantly higher among multilayered group.
DISCUSSION

Age
In our study, we found that the mean age of the study population was 28.77±4.95 (20.00-37.00) years. A study conducted by Chandra et al stated, “As a woman gets older, her chances of infertility increased among women aged 15 to 34 years, infertility rates ranged from 7.3 to 9.1%. In women aged 35 to 39 years old, the infertility rates increased to 25%. Lastly, women from ages 40 to 44 years had a 30% chance of infertility”.[13] In our study, pregnancy rate was significantly higher (62.02%) among <35 years who underwent full course of treatment, whereas it was relatively lower (42.85%) in women of age more than or equal to 35 years.

Endometrium
The size of the endometrium is directly proportional to the pregnancy outcomes. As the size increases, pregnancy rate improves.[14] In current study, the mean Endometrium at Baseline, Proliferative and secretory phase was 4.57±1.14, 6.69±1.05 and 7.86±1.38 respectively. Similar study by Khan MS et al.[14] and Kovacs et al.[15] also observed the same. In our study, the subjects with a multilayered type of endometrial appearance on transvaginal ultrasonographic evaluation had a successful pregnancy rate of 100% after the treatment. However, in patients with non-multilayered type of endometrium, only 25% of the patients showed positive UPT. A study by Khan MS et al[14] and Merc et al.[16] also reported the similar findings where the results showed pregnancy rate of 78.1% in multilayered (trilaminar) appearance of endometrium and 38.09% in hazy 5-line appearance of endometrium.[14]

A study by Zhao et al. reported that endometrial thickness and it’s morphology were independent predictors of pregnancy outcomes and the combination of two cannot be used as a predictor of IVF outcomes.[17] In our study, regardless of the endometrial thickness, the patients who showed multilayered type of endometrium had a successful pregnancy rate of 100% after the treatment. However, in patients with non-multilayered type of
endometrium, 25% of the patients showed positive UPT.

In our study, we observed that the infertility rates were higher in subjects with endometrial vascularity in Zone 1 (31.66%) and Zone 2 (36.66%). It was relatively lower in subjects with endometrial vascularity in Zone 3 (23.33%) and Zone 4 (8.33%). Out of the 36 patients who took the complete treatment for infertility, 21 females reported a positive UPT on subsequent follow up. We observed that the pregnancy rates were highest in patients with endometrial vascularity in zone 3 and zone 4, being 100% respectively with a p value of 0.001. Khan et al.[14] observed in their study that the pregnancy rates were significantly higher in endometrial vascularity zone 3. This was also backed up by Chien et al.,[18] where the results showed higher implantation and pregnancy rates in zone 3 i.e 24.2% and 47.8% respectively, whereas, zone 1 and 2 had lower rates of pregnancy i.e 28% and 30.7% respectively. It has been observed that a good endometrial vascularity can accelerate development of placenta during pregnancy which is affiliated with a lower risk of miscarriage and a better chance of live birth after taking ART.[14]

CONCLUSION

Transvaginal Color doppler examination can be a one-stop fertility assessment and cost effective measure of female infertility. The endometrial vascularity and appearance can be a dominant factor in predicting the outcome of pregnancy in women. However, additional Doppler investigations into physiological and pharmacological changes after the complete treatment in infertility is needed to assess the improved or unchanged uterine blood flow parameters.

REFERENCES


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