Section: Radiodiagnosis

Original Research Article

ROLE OF ENDOMETRIAL COLOR DOPPLER EVALUATION IN FEMALE INFERTILITY

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Abstract

Background: Uterine receptivity is an important aspect of the conception. Study of uterine perfusion using endometrial color flow in female infertility can provide significant information in subjects with unexplained infertility and can help target the same. Color doppler evaluation of endometrium provides useful information related to uterine perfusion which may be useful in the overall management of infertile females. The aim is to assess the role of endometrial Color doppler evaluation in infertile females. **Materials and Methods:** Our study included infertile females from 18-37years of age using strict criteria following approval from IEC. All the included subjects were evaluated for endometrial perfusion using color doppler on transvaginal sonography. In addition, B-modes findings of the endometrium were also recorded. Patients were followed up after taking treatment from TMU hospital to confirm the pregnancy results. The recorded data was then analyzed using appropriate statistical tools & methods. **Result:** The infertility was primary among 47 (78.3%) and Secondary among 13 (21.7%) subjects. Out of the 36 patients who took the complete treatment, Pregnancy rate was significantly higher (62.06%) among females with age < 35 years. The mean Endometrium at Baseline, Proliferative, and secretory phase was 4.57±1.14, 6.69±1.05, and 7.86±1.38 respectively. Pregnancy outcomes following the IVF treatment were significantly higher in endometrial vascularity zone 3 and 4 (100% respectively). **Conclusion:** Endometrial color doppler provides useful information related to the female infertility playing a crucial role in their management, hence should be a part of routine protocol in evaluation of such females.

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.[5] Since an adequate blood supply to the endometrium is an essential component of proper implantation,

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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.[6] This is particularly useful in situations when the cause of infertility cannot be explained.[7] 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.[8]

Transvaginal sonography combined with color Doppler evaluation, thus serves as an important tool for evaluation of female infertility since it is a relatively in expensive, safe, radiation free, non-invasive investigation, easy to use and easily repeatable approach to assess the uterine perfusion and changes in female reproductive physiology.[9,10]

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.[11]

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.[12] 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 Ultrasonography and Color Doppler in female infertility. The present study compared the Ultrasonography 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.[14]
  - ZONE 1- Myometrium surrounding the Endometrium
  - ZONE 2- Hyperechoic endometrial line
  - ZONE 3- Internal endometrial hypoechoic zone
  - ZONE 4- Endometrial Cavity

The treatment given to the patients before IVF was: Folic acid tablets, Ecosprin, Estradiol, Levonorgestrel 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.

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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

Endometrium	Mean	Std. Deviation	Minimum	Maximum
Baseline	4.57	1.14	2.80	7.00
Proliferative	6.69	1.05	3.80	8.60
Secretory	7.86	1.38	4.20	10.60

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

Endometrial Blood flow	No of cases	Type of Endometrium		T/T	No. of Pregnant cases	No. of Non- Pregnant cases	Pregnancy rate
		Non-multilayered	Multi-layered				
Zone 1	19	18	1	13	4	9	30.8%
Zone 2	22	18	4	11	5	6	45.5%
Zone 3	14	1	13	8	8	0	100.0%
Zone 4	5	0	5	4	4	0	100.0%
p-value		0.001*					

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

Table 4: Study population according to endometrial type

	Treatment taken		Pregnancy	
Multilayered	16	100.0%	16	100.0%
Non- Multilayered	20	100.0%	5	25.0%
p-value	0.001*			

Pregnancy rate was significantly higher among multilayered group.

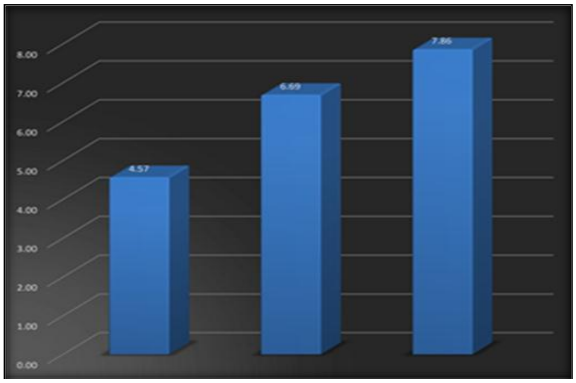

Figure 1: The mean Endometrium at Baseline, Proliferative and Secretory phase was 4.57±1.14, 6.69±1.05 and 7.86±1.38 respectively.

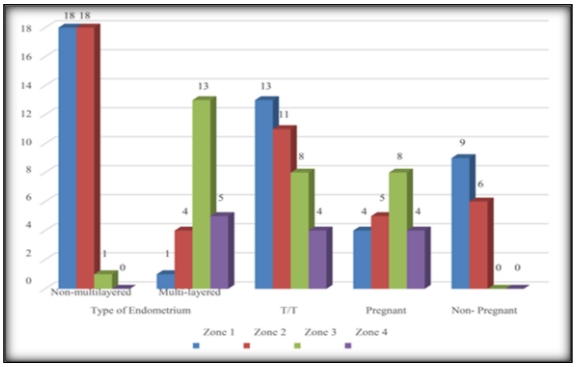

Figure 2: Bar graph depicting endometrial appearance, number of patients who took treatment and their pregnancy outcomes in respective Zones of vascularity. 100% pregnancy rates were seen in women with Zone 3 and 4 vascularity, respectively.

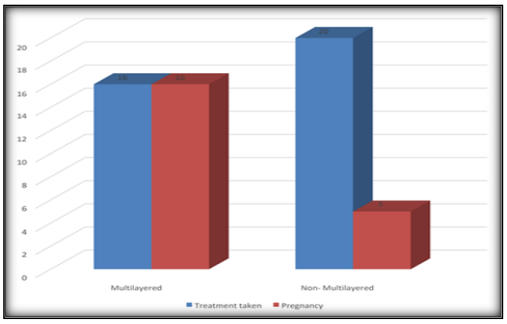

Figure 3: Pregnancy rate was significantly higher among multilayered group.

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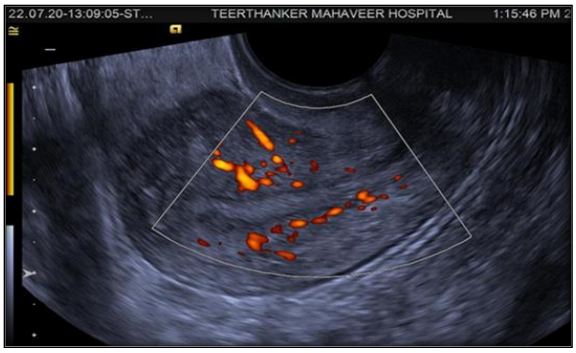

Figure 4: Endometrial blood flow in ZONE 1, i.e. the sub-endometrial region

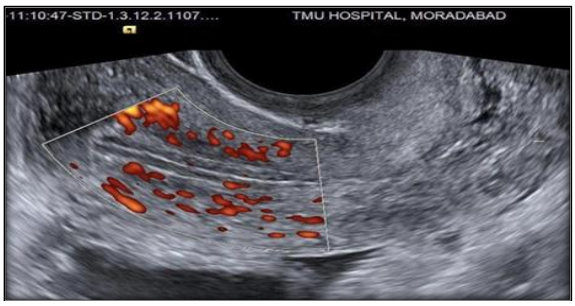

Figure 5: Endometrial blood flow ZONE 2 is the outer hyperechogenic zone

Case of a 28 yrs old woman with a successful fertilization outcome after taking treatment. Image shows a trilaminar appearance of endometrium in proliferative phase and measures approximately 4.7mm.

Figure 6: Endometrial Blood flow in the same patient showing ZONE 3 type of blood flow, i.e reaching upto the inner hypoechogenic zone

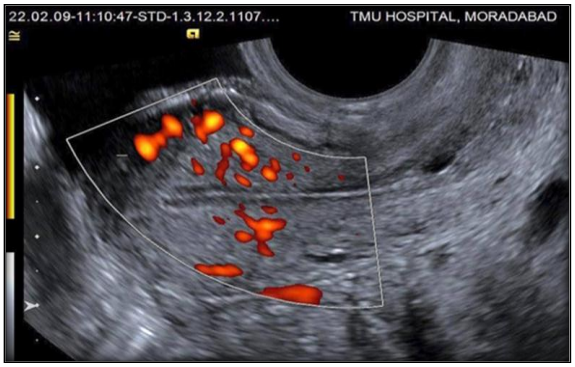

Figure 7: Endometrial blood flow in ZONE 4 in proliferative phase reaching upto the central hyperechoic layer

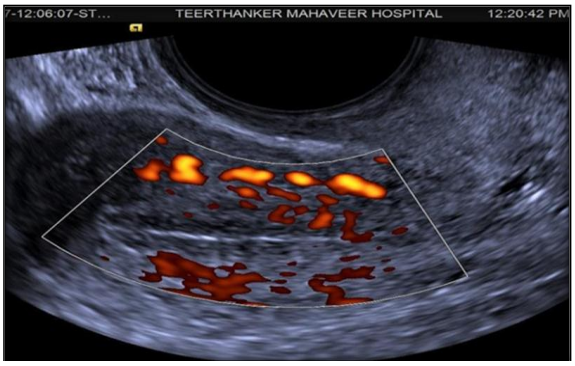

Figure 8: Endometrial blood flow in ZONE 4 in proliferative phase reaching upto the central hyperechoic layer

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

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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

1. Isaksson R, Tiitinen A. Present concept of unexplained infertility. Gynecol Endocrinol. 2004;18(5):278–90.
2. El-Shourbagy S, Ossman AME, El-Mohamady A. The role of sildenafil citrate (viagra) suppositories on endometrial response (thickness and mean resistance index of endometrial spiral artery) in cases of unexplained infertility. Menoufia Med J. 2017;30:343-9.
3. Raine-Fenning NJ, Campbell BK, Kendall NR, Clewes JS, Johnson IR. Endometrial and subendometrial perfusion are impaired in women with unexplained subfertility. Hum Reprod. 2004 Nov;19(11):2605-14.
4. Brugo-Olmedo S, Chillik C, Kopelman S. Definition and causes of infertility. Reproductive biomedicine online. 2001 Jan 1;2(1):173-85.
5. Habara T, Nakatsuka M, Konishi H, Asagiri K, Noguchi S, Kudo T. Elevated blood flow resistance in uterine arteries of women with unexplained recurrent pregnancy loss. Hum Reprod. 2002;17(1):190–4.
6. Rahman H. Role of Color Doppler and Three-dimensional Ultrasound in Infertility. Faridpur Med Coll J. 2018;13(1):97-100.
7. Ali zarad C, Mohamed MH, Shanab WSA. Role of uterine artery Doppler in assessment of unexplained infertility. Egypt J Radiol Nucl Med. 2021;52:(59).
8. Rastogi R. Role of imaging in female infertility (Dr. K.M Rai Memorial Oration Award). Indian J Radiol Imaging. 2010;20(3):168-73.
9. Uysal S, Ozbay EPÖ, Ekinci T, Aksüt H, Karasu S, Işık AZ, et al. Endometrial spiral artery Doppler parameters in unexplained infertility patients: is endometrial perfusion an important factor in the etiopathogenesis? J Turk Ger Gynecol Assoc. 2012;13(3):169–71.Devyatova EA, Tsaturova KA, Vartanyan EV. Predicting of successful implantation at IVF cycles. Gynecol Endocrinol. 2016;32(2):27-9.
10. Bhattarai M. Monitoring of ovarian follicular development and ovulation with transvaginal sonography (TVS) in infertile women in eastern region of Nepal. J Nobel Med Coll. 2016;5(1):43–8.
11. Bakos O, Lundkvist O, Wide L, Bergh T. Ultrasonographical and hormonal description of the normal ovulatorymenstrual cycle. Acta Obstet Gynecol Scand. 1994 Nov;73(10):790-6.
12. Hershko-Klement A, Tepper R. Ultrasound in assisted reproduction: a call to fill the endometrial gap. Fertil Steril.2016 Jun;105(6):1394-1402.e4.
13. Chandra A, Copen CE, Stephen EH. Infertility and impaired fecundity in the United States, 1982-2010: data from the National Survey of Family Growth. Natl Health Stat Report. 2013 Aug 14;(67):1-18, 1 p following 19.[PubMed: 24988820]
14. Khan MS, Shaikh A, Ratnani R. Ultrasonography and color doppler study to predict uterine receptivity in infertile patients undergoing Embryo Transfer. J Obstet Gynaecol India. 2016 Oct;66(Suppl 1):377-82.
15. Kovacs P, Matyas S, Boda K, et al. The effect of endometrial thickness on IVF/ICSI outcome. Hum Reprod. 2003;18(11):2337–41.
16. Merc LT, Barco MJ, Bau S. 2D and 3D power Doppler ultrasound of endometrium as implantation marker. Donald Sch J Ultrasound Obstet Gynecol. 2008;2(2):1–11.
17. 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;28(10):100.
18. Chien LW, Au HK, Chen PL, et al. Assessment of uterine receptivity by the endometrial-subendometrial blood flow distri- bution pattern in women undergoing in vitro fertilization embryo transfer. Fertil Steril. 2002;78(2):245–51.

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