ORIGINAL ARTICLE

# Role of 3D and 3D Power Doppler to Assess Endometrial Receptivity in IUI Cycles

**[1]Panchal Sonal Y, [2]Nagori Chaitanya B**

[1]Consultant Sonologist, Nagori's Institute for Infertility and IVF, Ahmedabad, Gujarat, India

[2]Nagori's Institute for Infertility and IVF, Ahmedabad, Gujarat, India

**Correspondence:** Sonal Panchal, Consultant Sonologist, Nagori's Institute for Infertility and IVF, 2nd Floor, Kedar Opposite Petrol Pump, Near Parimal Garden, Ahmedabad-380006, Gujarat, India, Phone: 07926402090, 9824050911 e-mail: sonalyogesh@yahoo.com

**ABSTRACT**

*Background:* The assessment of the endometrial receptivity at the time of human chorionic gonadotrophin (hCG) is one of the key factors for success of all ART procedures.

*Aim:* To assess, if 3D and 3D power Doppler assessment of endometrial receptivity before giving hCG, helps improving pregnancy rates in superovulation with IUI cycles.

*Settings and Design:* A prospective randomized study of 2500 cycles of IUI was done over a period of twelve months for pre-hCG endometrial assessment.

*Method:* Endometrial assessment was done on Voluson 730 Expert, (Wipro GE) using transvaginal multifrequency volume probe 5 to 9 MHz. When follicles and endometrium were considered mature by 2D US and color Doppler, 3D and 3D power Doppler assessment of the endometrium was done before giving hCG. These values were evaluated for conception and nonconception groups.

*Results:* Conception rates were higher, when endometrial volume was between 3 and 7 cc. In our study, we have found endometrial FI > 20 and endometrial VFI > 40 as most optimum.

*Conclusions:* 3D ultrasound is accurate for volume assessment of endometrium. 3D and 3D PD, when used with 2D US and color Doppler for pre-hCG endometrial assessment, it would definitely improve implantation rates in IUI cycles.

**Keywords:** Pre-hCG, Endometrial receptivity, 3D power Doppler.

## INTRODUCTION

The assessment of the follicular maturity and endometrial receptivity at the time of human chorionic gonadotrophin (hCG) is the key factor for success of all ART procedures.

Follicular maturity can be assessed by the assessment of oestradiol levels in blood as well as by ultrasound, but assessment of endometrial receptivity is possible by ultrasound only.

The accuracy of monitoring of infertility treatments such as ovulation induction has greatly increased because of the availability of sophisticated ultrasound (US) technology and equipment.[1] Since the advent of transvaginal ultrasound, this has been a preferred method for the assessment of follicle and endometrium. Invent of the Doppler in ultrasound has significantly improved the understanding of morphological changes occurring in the ovary and the uterus as a reflection of biochemical changes during the menstrual cycle.

Earlier the follicular size of 16 to 18 mm and the endometrial thickness of 8 mm were considered as appropriate for hCG administration for ovulation trigger. This is anatomical maturity of the follicle and the endometrium. But maturation of the follicle and the endometrium, ovulation and leutinization is a process of multiple biochemical, morphological and vascular changes. The vascular changes are reflection of the biochemical changes and can be studied by color Doppler. The spectral/pulse Doppler values give objective assessment of the follicular and endometrial vascularity. Therefore, color and pulse Dopplers speak about functional maturity of the follicle and endometrium. 3D ultrasound and 3D power Doppler assesses the global vascularity, as compared to vascularity in a single plane on 2D ultrasound and so may give better idea about follicular maturity and endometrial receptivity and therefore implantation rates.

## MATERIAL AND METHOD

This is a study of 2500 superovulation with intrauterine insemination cycles. Superovulation was done with gonadotrophins. Gonadotrophis used were recombinant or highly purified urinary follicle stimulating hormone (FSH). After US evaluation, gonadotrophins were started from the fifth day of the menstrual cycle.

Ovulation monitoring was done by B mode and Doppler using 5 to 9 MHz transvaginal volume probe, Voluson 730

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Expert, Wipro GE medical systems. Doppler settings were set at pulse repition frequency (PRF) 0.3, gain-8.0, wall filter lowest and balance 120. This included follicular and endometrial assessment. Follicular assessment included the diameter of the follicle on B mode scan and resistance index (RI) and peak systolic velocity (PSV) of perifollicular vessels on Doppler. Endometrium was assessed by transvaginal B mode US for its thickness and morphology. Endometrial thickness is measured on the longitudinal section of the uterus and at the thickest part of the endometrium. It is measured from the anterior margin of anterior hyperechoic layer to the posterior margin of posterior hyperechoic layer, excluding the hypoechoic endometrio-myometrial junctional zone. Doppler was used to assess RI and pulsatility index (PI) of the spiral arteries. Uterine artery PI was also assessed for all.

hCG was given, when follicular diameter was 18 mm, perifollicular blood vessels covered almost 3/4th of the follicular circumference and these vessels showed RI ≤ 0.48 and PSV ≥ 10 cm/sec. The endometrial thickness of ≥ 8 mm was confirmed. Apart from the thickness, multilayered endometrial pattern was essential. The morphology of the endometrium was further graded as the best, grade A. A triple line endometrium with the intervening area is as hypoechoic as the anterior myometrium. The echogenecity is attributed to the development of multiple vessels in the endometrium producing multiple tissue interfaces and causing the echogenecity due to the glycogen storage in the endometrial epithelium (Fig. 1). The endometrium is graded as intermediate or grade B (Fig. 2), when it is multilayered or triple line with the intervening area hypoechoic. Grade C or the most unfavorable endometrium would be a homogenous endometrium. Though some studies have shown no significant difference in pregnancy rates amongst different morphological patterns, we always preferred grade A or B endometrial morphology before giving hCG. A clear hypoechoic halo surrounding the whole endometrium, endometrio-myometrial interface is always ensured. Power Doppler was used to assess endometrial vascularity. The zones of vascularity are defined according to Applebaum[2] as: zone 1 when the vascularity on power Doppler is seen only in the myometrium surrounding the endometrium (Fig. 3), zone 2 when vessels penetrate through the hyperechogenic endometrial edge (Fig. 4), zone 3 when it reaches internal hypoechogenic zone (Fig. 5) and zone 4 when they reach the endometrial cavity (Fig. 6). We preferred zone 3 or 4 vascularity before giving hCG and confirmed these vessels had RI < 0.8 and PI < 2.3 (Fig. 7). Moreover, the pulse Doppler analysis of the uterine artery waveform was done. Uterine artery RI < 0.9 and PI < 3.2 were confirmed before hCG (Fig. 8).

When the endometrial and the uterine artery parameters were optimum as described above, the volume of endometrium with power Doppler was acquired and then the endometrial volume was calculated by VOCAL, tracing the outer edge of

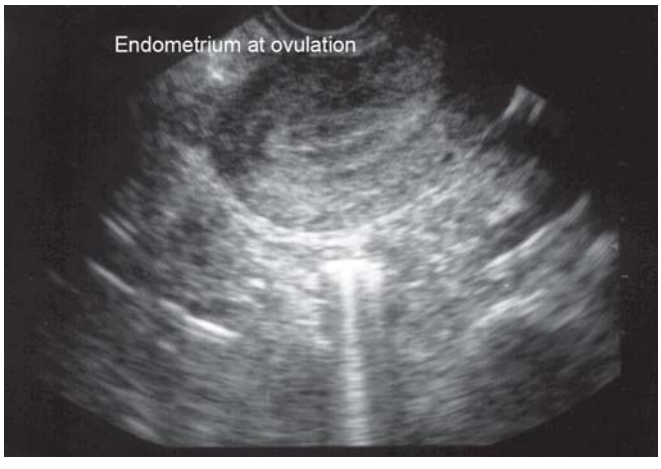



**Fig. 1:** Most receptive endometrium-multilayered

**Fig. 2:** Multilayered endometrium-intermediate

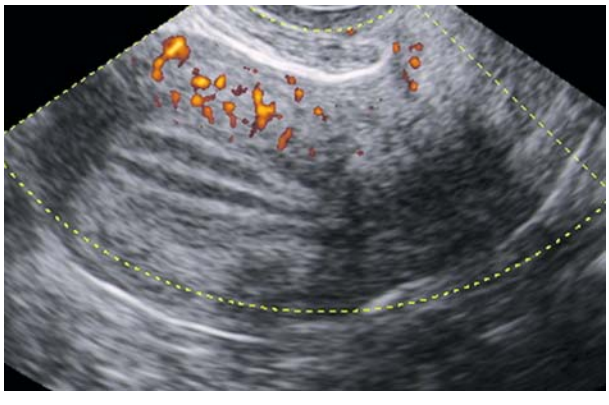


**Fig. 3:** Endometrial vascularity zone 1

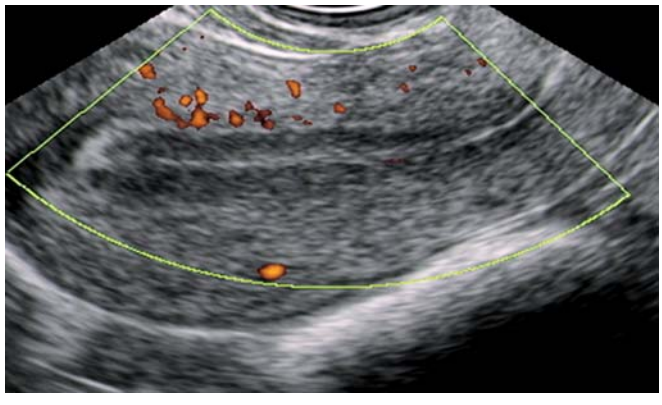


**Fig. 4:** Endometrial vascularity zone 2

the hyperechoic outer rim of the endometrium. The angle of the volume acquisition selected was large enough to cover the whole endometrium from edge to edge. The acquired volume was seen as endometrium in three perpendicular planes on the screen. Using the VOCAL (volume calculation by computer) software with 15° angle, the endometrium is traced at its circumference at every 15° rotation. At the end of the command 'done' given, the region of interest (ROI) is ultimately accepted. If any corrections are required they may be made and the machine then calculates the volume of the endometrium (Fig. 9). The endometrium upto the internal os was taken into calculation. For accurate measurements, a good contrast in the image is necessary. Select smaller angles of rotation for VOCAL.

Histogram was switched on to obtain vascularity index (VI), flow index (FI) and vascularity flow index (VFI) of the endometrium (Fig. 10). Volume histogram is a graph that shows the calculation of the gray voxels and the colored voxels in the given volume and these values are displayed on the screen as VI, FI and VFI values. VI indicates the abundance of the color voxels in the given volume, FI indicates the intensity of the color in the given volume and VFI is the ratio of the abundance and intensity, meaning it gives idea about the general perfusion status of the given volume.

Decision of time of hCG was based on follicular and endometrial maturity parameters based on B mode and Doppler ultrasound. hCG was given and IUI was done after 34 to 36 hours. Only those patients in whom post wash sperm count of 8 to 10 million was achieved were included in the study. Luteal support was given with 600 mg/day of micronized progesterone as vaginal suppositories. Urine pregnancy test (UPT) was done on 16th day of IUI and positive UPT was considered as desired and negative UPT was considered as undesired result.

Pregnancy rates were evaluated when compared with endometrial volume and endometrial VI, FI and VFI values.

## RESULTS

We have found only 8.3% pregnancy rates for zone 1 and 13.4% for zone 2 vascularity. The conception rates with zone 3 and 4 and the pregnancy rates were comparable and were 33.8 and 37.3% respectively.

Zone of vascularity (2500 cases)

| Vascular zone | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| Conc | 19 | 99 | 266 | 276 |
| Non Conc | 210 | 647 | 520 | 463 |
| Total | 229 | 746 | 786 | 739 |

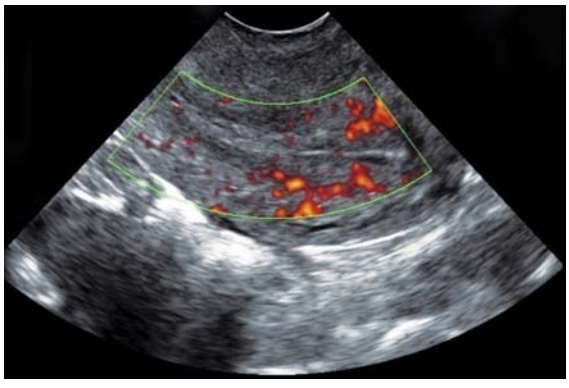


**Fig. 5:** Endometrial vascularity zone 3

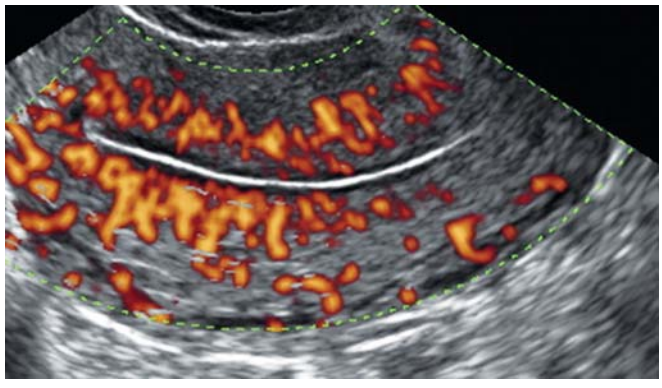


**Fig. 6:** Endometrial vascularity zone 4

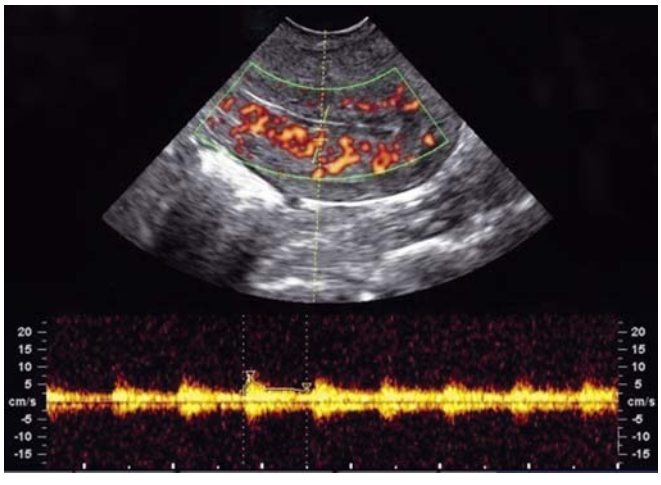



**Fig. 7:** Pulse Doppler of endometrial vascularity

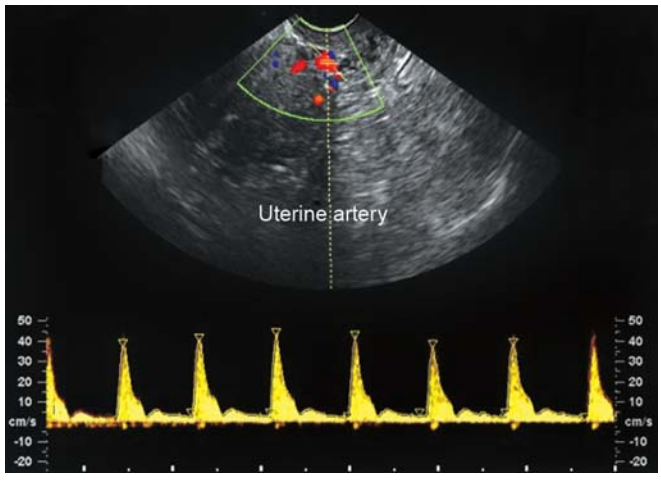



**Fig. 8:** Preovulatory uterine artery waveform

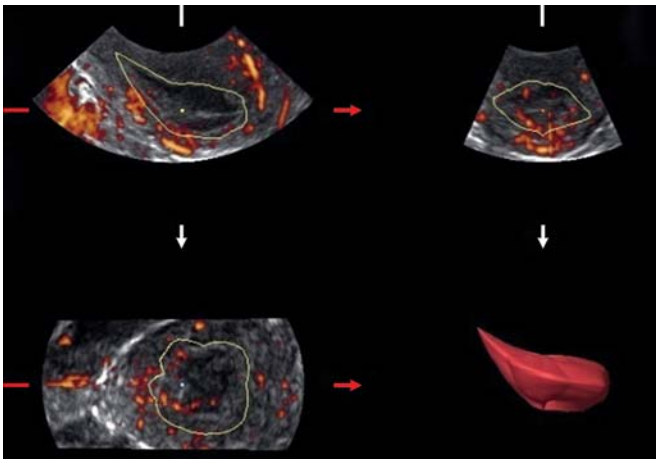


**Fig. 9:** Calculating endometrial volume by VOCAL

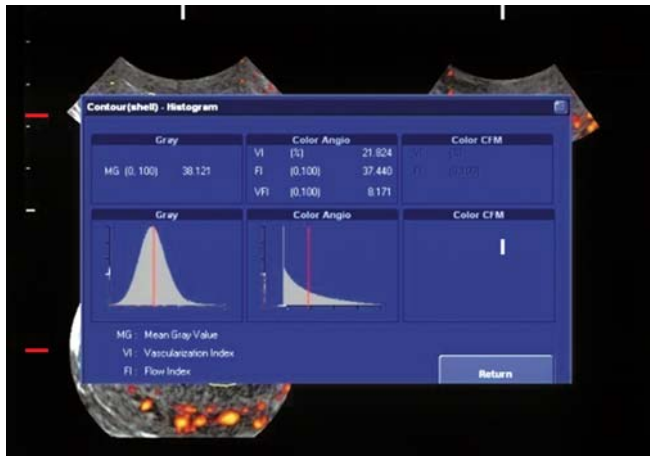



**Fig. 10:** Histogram of endometrium showing VI, FI and VFI values

On 3D, the endometrial volume of 3 to 7.5 cc has been found to be optimum in our study (Fig. 5).

Our study showed that at endometrial volume of < 2 cc no pregnancies occurred. With endometrial volume of 2 to 3 cc, only 16.66% of patients conceived between 3 and 5 cc 47% and when the endometrial volume was between 5 and 7 cc, 61.5% patients conceived.

Endometrial volume (2500 cases)

| Endo Vol | < 2 | 2-3 | 3.1-5 | 5.1-7 | > 7 |
|---|---|---|---|---|---|
| Conc | 0 | 130 | 350 | 335 | 205 |
| Non Conc | 100 | 660 | 390 | 210 | 120 |
| Total | 100 | 790 | 740 | 545 | 325 |

The endometrial VI values were not very conclusive. When Endometrial FI was < 20, only 23% of patients showed conception, between 20 and 40, it was almost 50% but when FI was more than 40, 68% of patients showed conception.

Endometrial FI (2500 cases)

| Endo FI | < 20 | 20-30 | 30.1-40 | > 40 |
|---|---|---|---|---|
| Conc | 185 | 340 | 375 | 170 |
| Non conc | 625 | 380 | 340 | 85 |
| Total | 810 | 720 | 715 | 255 |

When Endometrial VFI was > 20, the conception occurred in 71.2% of patients and when VFI was < 1.0, no conception was seen. Though between VFI 5 and 20, the percentage of conception was 49 to 56 % (Figs 11A to C).

Endometrial VFI (2500 cases)

| Endo VFI | < 2 | 2-5 | 5.1-12 | 12.1-20 | > 20 |
|---|---|---|---|---|---|
| Conc | 00 | 480 | 320 | 225 | 45 |
| Non conc | 220 | 680 | 330 | 180 | 20 |
| Total | 220 | 1160 | 650 | 405 | 65 |

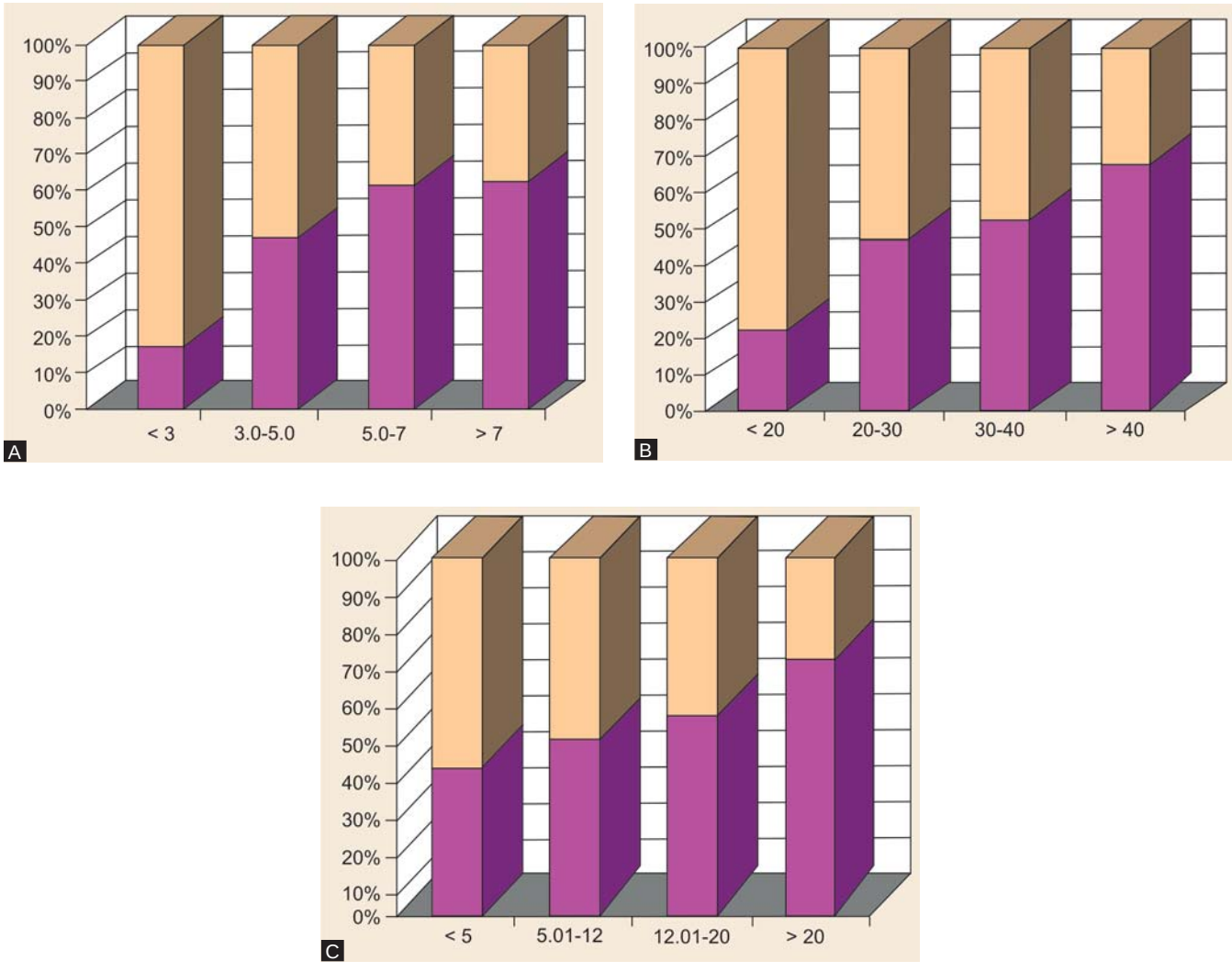
## DISCUSSION

Endometrial volume 3D US volume calculation of the endometrium may help to correlate the cycle outcome with quantitative parameter rather than endometrial thickness.[3] A study by Raga et al[4] shows pregnancy and implantation rates were significantly lower when endometrial volume was < 2 ml, while no pregnancy was achieved, when endometrial volume was < 1 ml. Study by Kupesic et al also shows no pregnancy when endometrial volume was < 2 ml, or when exceeded 8 ml.[5] Our results are comparable to these studies, and state an optimum endometrial volume from 3 to 7 cc. For endometrial volume, the inter CC definition of internal os and (interobserver variation) was 0.82 and intra CC (intraobserver variation) was 0.90, the chief source of error being definition of endometrial margins.[6]

Segmental uterine artery perfusion demonstrates significant correlation with hormonal and histological markers of uterine receptivity reaching the highest sensitivity for subendometrial blood flow[7]. The subendometrial blood flow corresponds to vascularity in zone 3 and zone 4 vessels which are endometrial vessels (Fig. 12). Zaidi et al found that absence of flow in the endometrial and subendometrial zones on the day of hCG indicate total failure of implantation.[8] In a study of 660 cycles by Chein et al, it was found that implantation and pregnancy rates were 24.2% and 47.8% respectively when endometrial and subendometrial flow was detected; 15.8% and 29.7% when only subendometrial flow was detected and 3.5% and 7.5% when neither subendometrial nor endometrial flow were registered.[9]

Volume histogram or the 3D power Doppler indices give the quantitative assessment of the vascularization and perfusion of the given volume. This gives a more global idea about the endometrial vascularity than the 2D power Doppler.

A scoring system reported by Kupesic et al[5] for uterine receptivity, done on the day of embryo transfer, shows that subendometrial FI < 11 was a cut off limit. No pregnancies occurred when it was < 11 and the conception group showed its values of 13.2 ± 2.2. These values of FI > 27 differ from our values probably because we have taken the whole endometrium as the volume as compared to the calculations made for the subendometrial layers here, but it is common in both that higher FI values are associated with higher pregnancy rates.




**Figs 11A to C:** Pre-hCG endometrial volume and 3D PD values (A) Endometrial volume (B) Endometrial FI (C) Endometrial VFI

Whereas Ng et al[10] documented a low endometrial VI and VFI in pregnant group on the day of oocyte retrieval and also a nonsignificant trend of higher implantation and pregnancy rates in patients with absent subendometrial and endometrial flow. This probably can be explained on the basis that hCG administration/LH peak causes increased uterine artery resistance and hence a decrease in endometrial perfusion on the day of oocyte retrieval. This also correlates with the observation made by Ng et al,[11] which says that subendometrial vascularization flow indices are significantly lower in patients with uterine artery RI ≥ 0.95. Though they concluded that a number of embryos replaced and the endometrial VFI were the only two predictive factors for pregnancy. Wu et al[12] reported that endometrial VFI was more reliable than VI and FI, and the best prediction rate was achieved by VFI cut off value of > 0.24.

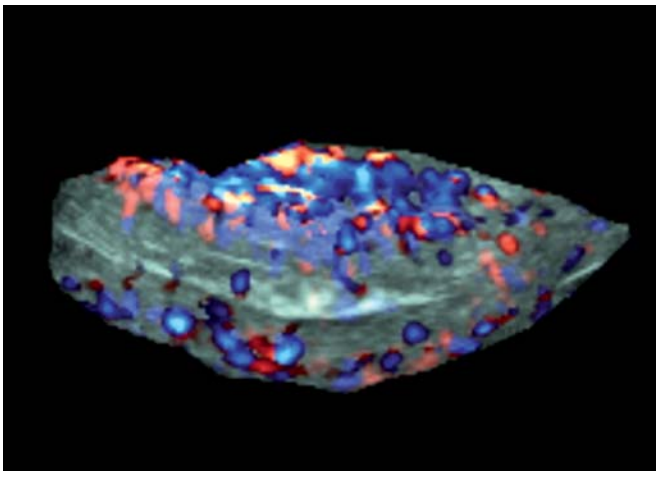


**Fig. 12:** Subendometrial and endometrial blood flow

## CONCLUSION

3D ultrasound is highly accurate for volume assessment of the endometrium, and a much more reliable parameter than endometrial thickness. The 3D power Doppler gives idea about the global vascularity of the endometrium. Though still larger studies are needed to establish more precise values for endometrial VI, FI and VFI, the results are fairly promising. We can hope to understand the endometrial physiological status better with these parameters and achieve better pregnancy rates with ART procedures and reduce the span of unexplained infertility.

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