

**ENDOMETRIAL CHARACTERISTICS IN
UNSTIMULATED CYCLES, AS STUDIED BY
TRANSVAGINAL GREY SCALE & COLOUR
DOPPLER SONOGRAPHY AND ITS IMPACT
ON PREGNANCY OUTCOME**

S. GHOSH DASTIDAR ● K. GHOSH DASTIDAR

SUMMARY

Endometrial echopattern is reported to be associated with pregnancy outcome (Gonen et al 1989). In the present series a prospective study involving 214 therapeutic donor insemination (TDI) cycles were subjected to grey scale, colour and pulsed Doppler ultrasonography in proliferative phase and the final pregnancy outcome was analysed among the different varieties of endometrium studied namely A, B, C types. 20.8% pregnancy per cycle was achieved in the B2 type of endometrium. Poor responder in terms of possible endometrial receptivity to implantation was seen to be the C Group.

Our study indicates that B2 type endometrium is associated with higher pregnancy rate. We conclude that detailed study of this endometrial echocharacter during the follicular maturation phase could be of prognostic value in terms of pregnancy outcome of a particular treatment cycle.

INTRODUCTION

Hormone levels in peripheral blood can guide towards maturation of follicles and

subsequent ovulation. The physiological maturation of the endometrium through the proliferative phase, associated with rising level of E2 in blood, could not be studied non-invasively before the advent of ultra-

sound. But recently it has been suggested by Santolaya - Forgas (1992), that the approximate day of a normal woman's menstrual cycle can be ascertained by the ultrasound appearance of her endometrium. The addition of transvaginal sonography in gynaecological practice has changed the picture greatly and a detailed appraisal of endometrial 'sonophysiology' is now possible. A correlation between endometrial thickness, echopattern and successful pregnancy in stimulated cycles has been studied with grey scale and Doppler ultrasound by workers like Glissant et al, (1985) Welker et al (1989) and Smith et al (1984). Our study involves unstimulated cycles of otherwise normal females.

AIMS AND OBJECTIVES

Our aim was to prospectively study endometrial echopattern in infertile patients by grey scale and Doppler ultrasound as reported previously by Applebaum (1993); in the proliferative phase, of unstimulated cycles with special reference to its characteristics on the day of ovulation; and correlate subsequently with serum progesterone (P) on 8th day of ovulation and pregnancy in that cycle after therapeutic donor insemination (TDI). The main aim of this study was to standardise the different normal patterns of endometrium in unstimulated cycle with pregnancy rate to explore the potential of this data in prediction outcome based on USG characteristics in ART cycles.

METHODS

214 cycles of previously detected normo-ovulatory patients with azoospermic husbands booked for therapeutic donor

insemination (TDI), were studied between December, 1993 and June, 1995. Mean age of female partners was 30 years (range 26 to 34 years 8 months). The machine used for grey scale follicular and endometrial studies was Philips SDR 1550 X P with 5/7.5 MHZ transvaginal probe and Ultramark 9 (ATL) for transvaginal colour and pulsed Doppler. Each examination took about 30-45 minutes and were performed by a single observer (KGD). Investigations had previously shown normal level of FSH, LH on Day-3 of menstrual cycle and normal serum, PRL and TSH, in previous mid follicular estimation, in these patients. Basal ultrasound study was started on Day-3-4 to get normal echotexture of post-menstrual endometrium. 7 patients showing endometrial pathology like polyp, synechia etc were excluded from the study, Daily monitoring of endometrium was started on Day-7 till the day of ovulation as detected by real time. Ovulation was said to have occurred when

(a) a track of fluid was seen to be coming out of the follicle. This was named as "track-sign" by us.

(b) the size of follicle as measured by its diameters in its three dimensions was seen to have decreased from previous day;

(c) the complete disappearance of the follicle was noted.

In 2 patients the size of the follicle was seen to be same with echographic changes of the follicular character. This, associated with secretory-like change referred previously by Hackeloc (1984), in the endometrium led to the possible diagnosis of luteinised unruptured follicle (LUF) and these cases were excluded from the study. In 7 cases more than one follicle was seen

to grow to 13 mm on the same day, these were also excluded. The endometrium was studied in the long axis and its thickness was measured by placing the electronic callipers at the anterior and posterior endometrial-myometrial interphase. Measurements were recorded in millimeters. Three varieties of echo type were distinctly noted :

TYPE - A, when a hyperechoic endometrium (Fig 1) resembling the echocharacter seen in the normal 'secretory phase' of the endometrium with loss of central line was seen.



Figure 1. Type 'A' endometrium - Hyperechoic with loss of central line.



Figure 2. Type 'B' endometrium-Multilayered showing homogeneously granular appearance.

TYPE - B, when a homogenous echopattern giving the endometrium a predominantly granular appearance, in association with some internal hypoechogenicity is seen (Fig 2).

TYPE - C, when three distinct layers of endometrial echo is seen, with predominantly hypoechoic area in between these layers (Fig 3).



Figure 3. Type 'C' - endometrium-Multilayered showing internal hypoechogenicity.

Each grade was subdivided into thick and thin variety depending on whether they were less than 8mm or more than 8mm on day of ovulation and were classified as A1, A2, B1, B2 and C1, C2 respectively. Doppler studies, both pulsed and colour was started when the dominant follicle reached a transverse diameter of 13 to 14mm. The endometrial, subendometrial flow was first studied by colour Doppler, and then by velocimetric study, setting the filter approximately at 100 Hz. Such velocity wave forms (Fig 4) were studied at different sites within the subendometrium/endometrium daily wherever good flow was recorded and their mean recorded for the day. Progressive vascularisation towards the

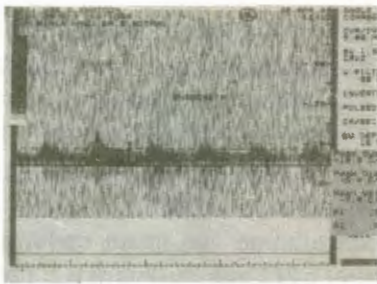


Figure 4. Pulsed Doppler Velocimetric Tracing of Endometrial Artery.

endometrial canal was also detectable by colour Doppler in some patients with passage of days. The parameter studied were peak systolic flow, (S) peak diastolic flow (D) pulsatility index, (PI) and resistance index (RI). Serum E2 was measured in peripheral blood drawn on day when follicle had transverse diameter >17mm.

Serum Progesterone (P) was estimated on 8th day following ovulation.

RESULTS ANALYSIS

The result of TDI were analysed taking cumulative pregnancy rate during 3-6 treatment cycles. Out of the 198 cycles studied prospectively, serum beta hCG was positive for pregnancy in (1) none out of 4 in group A1. (2) 1 out of 18 (5.5%) in Group A2; (3) 1 out of 44 (2.2%) in Group B1; (4) 19 out of 91 (20.8%) in Group B2; 1 out of 23 in Group C1 and (4.3%); (6) 2 out of 18 (11%) in Group C2. The number of first trimester abortions were 1 in Group A2, 1 out of 1 (100%) in Group B1, 2 out of 19 (10.5%) in Group B2 and 1 in Group C2. 1 patient of Group B2 had an early second trimester abortion due to cervical incompetence and the other had premature rupture of membrane at 32 weeks delivering 1980 gm baby and the neonate survived. PI of endometrium on

Table 1

Endometrial Echo type	Number of Cycle	Mean Pulsed Doppler Values of endometrial/sub-endometrial flow on day of ovulation				Serum Progesterone level 8 days after ovulation (mg/ml)	Number of Pregnancy in each endometrial type	Number of Abortion
in (nm)		Peak Sys. Dopp. Shift (cm/sec)	Peak Diast. Dopp. Shift (cm/sec)	Pulsatility Index (PI)	Resistance Index (RI)			
A1 <8	4	4.8	2.5	1.56	0.82	5.2 (range 4.5-5.9)	0	0
A2 >8	18	12.3	8.7	1.38	0.97	7.5 (range 5.3-9.7)	1(5.5%)	1
B1 <8	44	10.2	4.3	0.99	0.58	9.3 (range 8.2-10.4)	2(2.2%)	1
B2 >8	91	5.3	4.7	0.76	0.66	40.4 (range 21-68.4)	19(20.8%)	4
C1 <8	23	9	6.5	1.26	0.91	8.5 (range 5-12)	1(4.3%)	0
C2 >8	18	4.1	2.7	0.79	0.52	20.8 (range 19.4-22.5)	2(11%)	1

day of ovulation was significantly low in varieties of endometrium giving higher pregnancy rate. (P) values in cycles showing thicker endometrium on day of ovulation was also comparatively higher though E2 level of all the patients did not vary significantly and was between 125-210pg/ml.

DISCUSSION

An enormous amount of knowledge about the endometrial character has been understood in recent years which could mostly be credited to the advent of newer modalities amongst which diagnostic sonography finds a place of privilege. This advancement, particularly with respect to Doppler studies is still being studied intensively.

The cyclical nature of reproductive organs in the female is unique in its own way, largely due to the intricately co-ordinated function of hypothalamic - pituitary ovarian axis leading to production of the key hormone estradiol 17B from the maturing follicle, resulting in marked growth of endometrial thickness. Like the endometrium, its spiral artery blood flow has also been seen to respond to cyclical endocrinal variations. In our study, involving 198 normo-ovulatory cycles, different varieties of endometrial pattern studied, showed preponderance of the homogeneously echogenic type that reached a mean thickness of 12mm on day of ovulation. This type named B2 by us, was seen in 91 cases (45.9%) amongst all and was also seen to have the highest pregnancy rate per cycle (20.8%). The next common was B1 (22.2%) with a mean thickness of 7 mm on day of ovulation. This variety was subsequently seen to contribute only 2.2% in the pregnancy rate.

C1 variety was seen in 23 (11.6%) and had 4.3% success in term of pregnancy. C2 variety which was seen in 18 (9.09%) cases showed an average thickness of 13mm, on day of follicular rupture and gave a pregnancy rate of 11%.

If we compare the mean endometrial thickness of C2(13mm) to that of B2(12mm), it is tempting to conclude that it is the echopattern which is more important than the thickness of endometrium in terms of pregnancy rate. This finding is in agreement with that reported by Welker et al (1989) but not supported by the work of Richard Dickey et al (1993) and his co-workers.

The other variety of hyperechoic 'secretory-like' endometrium is proliferative phase was seen in Group A1 (2.0%) and Group A2 (9.09%). However we could not explain the etiopathology of such 'secretory' like endometrium in proliferative phase of this subset. Premature leuteinisation could be a plausible explanation of such effect. Since progesterone levels in late proliferative phase was not measured in the current study, we cannot make any comment in this regard. Nevertheless, it is well known that premature leutinisation on day of WCG in IVF cycles, is associated with poor fertilisation and pregnancy rate. In terms of pregnancy the most successful was the B2 type followed by the C2. The A1 variety was the worst with reference to pregnancy outcome. However, the number of cycles with this echocharacter was small to comment conclusively.

With respect to doppler studies the colour flow was studied daily from day 7 of the cycle and its forward progression previously reported by Applebaum (1993) towards

the endometrial canal was observed. Possibly this signified the growth of the spiral arteries. Pulsed Doppler studies of these vessels were undertaken simultaneously. Amongst all the velocimetric parameters studied; pulsatility index, (PI) first explained by Gosling and King; as a measure of the systolic diastolic, differential of the velocity pulse, appears to be a useful way of expressing blood flow impedance distal to the point of sampling (Bourne et al 1989) and it was studied carefully. The values of PI obtained through the cycle is recorded in Table I. In our series, the lowest value of PI recorded on day of ovulation or just prior to it was in Group B2 which showed highest pregnancy rate. Relationship of uterine artery pulsatility index and accurate artery pulsatility index and pregnancy in IUI cycles has shown that pregnancy occurred in patients showing lower PI values on day of hCG injection (Jong-chow Chang et al 1993). Our study done in unstimulated ovulatory cycle also indicates that, thickness of endometrium, its echo type and its pulsatility index on day of ovulation has a significant relation to pregnancy in that cycle.

CONCLUSION

We conclude that careful study of endometrium especially the echotexture as described in our study, appears to bear a strong co-relation with final pregnancy outcome in natural cycles. Such variations in endometrial pattern in spite of ovulatory cycle, remains a mystery. Moreover, combining parameters other than endometrial thickness alone, will probably improve the

predictive value of endometrial receptivity. It is worth studying the echo types to investigate whether the poor responder, to endogenous ovarian stimulation seen here show improvement of endometrial echopattern by "echo conversion" (eg. A->B or C1->C2) and pregnancy outcome with treatment. A study is also being designed to see if cases of 'non-progression of forward endometrial vascular flow' will be converted to 'progression of flow' cases with treatment. If so, we are also eagerly waiting to see if improvement in pregnancy outcome occurs in such cases, not only in natural cycles but also in stimulated cycles undergoing IVF and other ART procedures.

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