

ULTRASONOGRAPHIC EVALUATION OF ENDOMETRIAL THICKNESS; HOW RELEVANT IN FEMALE INFERTILITY ASSESSMENT?

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ABSTRACT

Background: The endometrium is vital for successful conception. Two dimensional ultrasound (2-D US) can be used to assess the endometrial thickness at different phases of the menstrual cycle. However, ultrasonographic measurement of the endometrial stripe in females with infertility on the day of hysterosalpingography (HSG) which in our environment coincides with the proliferative or late follicular phase of the menstrual cycle, will result in standardization of the menstrual timing of such a study. **Aim:** To ascertain the usefulness late follicular phase ultrasonographic evaluation of endometrial thickness in infertility assessment. **Study design:** A prospective cross sectional descriptive study. **Methods:** A total 127 subjects were scanned and endometrial stripe thickness were analyzed with the statistical package for social sciences version 21; $P \leq 0.05$ being considered statistically significant. **Results:** The ages ranged from 20-49 years with mean of 32.5 ± 5.2 , while the endometrial thickness ranged from 0.1-16.0mm with mean of 2.2 ± 2.2 and measurement of $<4\text{mm}$ in 93.7% of the subjects. There was significant correlation between the endometrial thickness and the duration of infertility, parity, and the duration of last episode of dilatation and curettage (D&C); but no significant correlation between endometrial thickness and the age of the subjects, the age at menarche, the type of infertility and the duration of menses. **Conclusion:** The endometrial thickness of most of the subjects was below the normal range of follicular phase endometrial thickness. This implies that endometrial thickness is relevant in female infertility assessment.

KEYWORDS: Infertility, ultrasonography, endometrial thickness.

INTRODUCTION

The endometrium plays a key role in successful conception by providing the site for implantation of the blastocyst and supporting the developing embryo and fetus.^[1] Pelvic ultrasound with transabdominal and transvaginal techniques is the preferred imaging technique in the study of the endometrium.^[2,3] Further evaluations are done with sonohysterography and magnetic resonance (MR) imaging.^[2,3]

Two dimensional ultrasound (2-D US) has been used to study the various changes in endometrial thickness through the menstrual cycle both in natural cycles and in hormonal stimulation.^[4,5] It has been opined that endometrial volume measurement with 3-D US is not superior to endometrial thickness measurement with 2-D US in predicting the outcome of assisted reproductive

technique (ART) and as such the former should not be used for routine clinical practice.^[4]

The endometrium is noted to be thinnest immediately after menstruation, measuring 1-4mm, increasing through ovulation and reaching maximum at the luteal phase.^[2,3,6] During the proliferative phase of the endometrial cycle (which is also the follicular phase of the ovarian cycle), it measures 4-8mm, at the time of ovulation it has a trilaminar appearance and measures up to 11mm.^[2,3] during the 2nd half of the endometrial cycle which is the secretory phase, it is uniformly echogenic and can measure up to 14mm.^[2,3] During this secretory phase it may even measure up to 16mm.^[6]

Despite the controversies in the reviewed literature over the prognostic value of endometrial thickness in

achieving conception, most authors noted that the endometrium was statistically thicker in fertile females than infertile ones.^[1,7,10]

In the investigation of premenopausal women for infertility, hysterosalpingography (HSG) which is a foremost investigations is commonly carried out in compliance with the ten day rule.^[11,12] This coincides with the late follicular phase. Ultrasonic measurement of the endometrial stripe on the day of the HSG in this population will make for standardization of the menstrual timing of such a study.

In this study, we carried out this standardized study and compared the results between subjects with primary and secondary infertility. We also compared the results with those obtained from females with infertility and from fertile women in other centres.

METHODS

This prospective descriptive study was carried out at the Department of Radiation Medicine of two tertiary specialist centres in South Eastern Nigeria. Ethical clearance was obtained from the relevant authorities prior to the study.

Women being managed for infertility, who were booked for HSG or for both HSG and TAUS in either of the institutions, and who gave their consent to be included for the study were consecutively recruited. Those booked for other reasons than infertility, those whose endometrial stripe could not be visualized as well as those whose data were not complete and those with gross endometrial pathologies, were all excluded from the analyses.

Hysterosalpingography was booked in compliance with the ten-day rule which coincided with the proliferative (follicular) phase and TAUS was performed on the same day before the HSG. Two dimensional, transabdominal ultrasonography was carried out on each subject using an ALOKA ultrasound machine fitted with a curvilinear probe of 3.5-5.0MHz frequency. A clear water-based gel was applied over the pelvic area for acoustic coupling and both sagittal and transverse scans were performed. Measurements of the endometrial thickness were taken at sagittal views as shown in figure 1.

The Statistical Package for the Social Sciences (SPSS) version 21.0 by IBM Corp. Armonk, New York, USA

was used for the analyses. Scale categories (quantitative data) e.g. endometrial thickness of the subjects, were analyzed using simple frequency table, and further by both the measures of central tendencies (mean, median and mode) and dispersions (range and standard deviation). Binomial nominal categorical data (like presence of heavy flow, presence of scanty flow) were analyzed using binomial test for significant proportions based on Z approximation. Paired numerical / nominal categories were tested for paired sample correlation. P-value ≤ 0.05 was considered statistically significant.



Fig. 1: Longitudinal image of the uterus showing the endometrial stripe.

RESULTS

A total of 200 subjects were recruited for the study. The endometrial stripe was either not visualized or grossly distorted in 73 subjects and they were excluded in the analysis. Of the 127 subjects analyzed, the age ranged from 20-49 years with mean of 32.5 ± 5.2 . Those within the age range of 25-39 years constituted 86.7%. The mean age at menarche was 14.1 ± 1.6 years with a minimum and maximum ages of 10 and 19 years respectively. While 16.5% had the primary type of infertility, 83.5% had the secondary type. The duration of infertility ranged from 1-18 years with mean of 3.9 ± 3.0 . The mean duration of menstrual flow of the subjects was 3.6 ± 0.9 days while the range was 2-6 days.

Thickness of the endometrium in the subjects ranged from 0.1-16.0mm as seen in table 1, with mean of 2.2 ± 2.2 . Majority (70.9%) of the subjects had endometrial stripe thickness of the range of 0.1 – 2.0mm. The endometrial thickness was $<4\text{mm}$ in 93.7% with the least measuring 4.1-6.0mm.

Table 1: Frequency distribution of endometrial thickness.

Endometrial thickness (mm)	Frequency	Percent	Valid Percent	Cumulative Percent
0.1-2.0	90	70.9	70.9	70.9
2.1-4.0	29	22.8	22.8	93.7
4.1-6.0	1	.8	.8	94.5
6.1-8.0	3	2.4	2.4	96.9
8.1 AND ABOVE	4	3.1	3.1	100.0
Total	127	100.0	100.0	

While there was a statistically significant correlation between the endometrial thickness and the following: the duration of infertility, parity, and the duration of last episode of dilatation and curettage (D&C) as seen in Table 2; there was a negative correlation between the

endometrial thickness and the number of previous miscarriages. No significant correlation was noticed between the endometrial thickness and the age of the subjects, the type of infertility, the age at menarche, and the duration of menstrual flow.

Table 2: Correlation between endometrial thickness and some variables.

Variables	Correlation coefficient	P-value
Duration of infertility	0.262	0.004
Parity	0.196	0.032
Number of previous miscarriage	-0.205	0.025
Duration of Last episode of D&C	0.458	0.000

DISCUSSION

The mean follicular phase endometrial thickness of 2.22mm in our study was less than the mean of 2.78mm and 3.58mm found by Kumar et al.^[1] in the postmenstrual phase of infertile and fertile women respectively. It was also less than the means of 7.78mm and 9.72mm respectively recorded by them in the mid-cycle of those subjects. Since both researches involved only premenopausal women who were not under ovarian stimulation at the time of the investigations, the differences may be due to the fact that their study excluded those with any form of operative manipulation but ours included those with history of previous dilatation and curettage (D&C) which is an operative manipulation. Again, since ours was carried out in Nigeria and theirs in India, racial influence on endometrial thickness is a possibility to be considered.

The endometrial thickness of 92.9% of our subjects was less than 4mm and that of 64.6% was less than 2mm. Since the normal proliferative or late follicular phase endometrium thickness is within 4-8mm,^[3] this suggests that low endometrial thickness may be contributory to infertility in our subjects. This position was further supported by a study that found the mean endometrial thickness to be significantly lower in infertile than fertile women in all the three phases of the menstrual cycle of women without ovulation induction,^[1,13,14]

Concerning infertile women undergoing ovarian stimulation with Clomiphene citrate; while a study showed that pregnancy was not achievable if the endometrial thickness remained less than 6mm,^[15] another study found no significant difference in pregnancy rates among those with endometrial thickness less than 6mm and those more than 6mm.^[16]

On the other hand, a different study found that in patients undergoing stimulation with human chorionic gonadotropin (HCG) for fresh in-vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI), endometrial thickness was one of the independent variables predictive of clinical pregnancy and that no pregnancy was achieved when the thickness was below 4mm.^[8] This implies that with majority of our subjects having less

than 4mm, the prognosis of conception even with assisted reproduction is reduced.

Baradwan et al,^[17] observed that among patients with hysteroscopic adhesiolysis for Ashermann’s syndrome, those with endometrial thickness >5mm at mid cycle achieved statistically more pregnancy rates than those with ≤5mm. From the fore going, the endometrium thickness of <2mm in 64.6% and <4mm in 92.9% of our subjects is a source of concern.

There was no significant correlation between endometrial thickness and age of the subjects in our study. Similarly, using a different modality (Sonohysterography), a study in Texas, USA, found no statistical difference between the median ages of premenopausal women with follicular phase endometrial thickness less than 5mm and those ≥ 5mm.^[18] Another study with TVS found no relationship between the endometrial thickness and the ages of premenopausal patients presenting for cervical cancer screening in China.^[19] It follows from the above findings that on ultrasound, the endometrial thickness of premenopausal women did not significantly vary with their ages regardless of whether the measurement was with 2-D US, sonohysterography or TVS.

There also appeared to be no racial influence on the endometrial thickness among premenopausal women since the results above were obtained from three different continents (Africa, North America and Asia respectively).

Whereas our study found a correlation between endometrial thickness and parity among premenopausal women, Hebbar et al.^[20] noted in a study of postmenopausal women, that the endometrial stripe was thicker among the nulliparous.^[20] They attributed the result obtained among the postmenopausal women to the effect of long period of unopposed estrogen stimulation with no intervening normal cycle.^[20] In our study population, this long unopposed stimulation by estrogen was not applicable. This is because rise in estrogen level during the proliferative phase with rise in both estrogen and progesterone levels during the secretory phase and eventual decline of both hormones caused the building

up and the shedding of the endometrial lining during each cycle in premenopausal women.^[21]

The negative correlation of endometrial thickness with the number of previous miscarriages in our study implies that lower endometrial thickness was found among subjects with higher number of previous miscarriages. This is in keeping with the finding by Yuan *et al* who observed that among women who conceived following HCG stimulation that the endometrial thickness of those who achieved life birth was significantly thicker than those that ended up in spontaneous abortion.^[8] However Kovacs *et al.*^[10] found no such significant difference. From our study, it appears that low thickness of the endometrial stripe is contributory to infertility and miscarriage among the subjects.

The correlation between endometrial thickness and duration of the last D&C may be due to physiological recovering and rebuilding of the endometrial lining (and hence thickness) over time. Hence the longer time after the last D&C would have allowed the endometrial thickness to recover as much as possible from the surgical intervention.

CONCLUSION

The findings in this study supports the idea that thin endometrial stripe contributes to infertility and miscarriage among premenopausal women. The endometrial thickness of most of the subjects was below the normal range of follicular phase endometrial thickness. Endometrial thickness also further identifies patients who are likely to benefit maximally from assisted reproduction which is quite expensive and needs proper preparation to reduce failure rates and reduce financial burden in a resource poor economy. This implies that endometrial thickness is relevant in female infertility assessment and should continue to be encouraged as part of the early fertility work-up.

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