Original Article

Role of Ultrasound in Assessment of Endometrial Thickness in Secretory Phase of Infertile Females

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ABSTRACT

Infertility in women is caused by a variety of hereditary and acquired uterine problems. Ultrasound has been found to be a good, quick, safe, and cost-effective way to assess the size, quantity, and location of abnormalities and to measure endometrial thickness in different phases of menstrual cycle **Objective:** To evaluate the role of ultrasound in assessment of endometrial thickness in infertile females of secretory phase. **Methods:** This is a descriptive study, including eighty-two females age 24 to 46 years from University ultrasound clinic, Lahore after the approval of ethical committee of Faculty of Allied health sciences, The University of Lahore. Informed consent was taken before including the subjects in the study. Data was collected according to data collection sheets. **Results:** The results showed that primary infertility (54.9%) is more in females than secondary infertility (45.1%). There were 10(47.6%) females in primary infertility with 9-12mm endometrial thickness and 11(52.4%) in secondary infertility. 24(57.1%) females in primary infertility with 13-16mm endometrial thickness and 18(42.9%) in secondary infertility. 11(68.8%) females in primary infertility with 17-20mm endometrial thickness and 5(31.3%) in secondary infertility. 3(100%) females in secondary infertility with 21-24mm endometrial thickness **Conclusions:** Female patients who initially taking infertility treatment had less endometrial thickness in proliferative phase; their endometrial thickness maybe increased in early secretory phase or at 21st day of their menstrual cycle but they had lost their chance to conceive the pregnancy in proliferative phase due to less endometrial thickness. The females should know the normal endometrial thickness in different phases of their menstrual cycle to conceive the pregnancy. This study shows that ultrasound plays a vital role in detecting endometrial thickness in infertility treatment.

INTRODUCTION

Infertility is a frequent problem that affects approximately 10-15% of all couples worldwide. Infertility in women is caused by a variety of hereditary and acquired uterine problems [1]. Infertility is described as a couple's inability to conceive despite multiple unprotected efforts over a 12-month period [2]. Female infertility has a variety of causes, which can be categorized into organic and functional categories [3]. Endometrial thickness is measured from echogenic border to echogenic border. During menstruation, the endometrium appears as a thin, echogenic line 1– 4 mm in thickness. Once the proliferative phase of the menstrual cycle (days 6 –14) begins, the endometrium becomes thicker (5–7 mm). In the late proliferative phase, the endometrium may measure up to 11 mm in thickness. During the secretory phase, the endometrium becomes even thicker (7–16 mm) and more echogenic [4]. The ultrasound examination for endometrial pathology includes a measurement of endometrial thickness. In clinical studies, endometrial malignancy is uncommon in women with an endometrial thickness

measurement <5 mm [5]. Following a comprehensive clinical examination, ultrasonography (USG) is usually the first investigation conducted on an infertile female [6]. Many studies have proposed that a correlation exists between endometrial thickness and uterine receptivity with significantly higher pregnancy rates the greater endometrial thickness [7]. Many factors add to attaining a successful pregnancy. Understanding these aspects can help in counseling patients about their chances of success and in proposing interventions for improvement [8]. With respect to endometrial difference, the potential predictors of pregnancy that have been assessed are endometrial blood flow, endometrial pattern, and endometrial thickness [9]. Endometrial thickness has been weighed as a potential predictor of pregnancy in numerous studies with conflicting results [10]. Some studies have shown no changes in pregnancy rates with respect to endometrial thickness [11]. Rinaldi *et al.* observed decreased pregnancy success with thin endometrial linings (<10 mm) on the day of hCG administration [12]. Others have found opposing data in evaluating thicker endometrial linings on the day of hCG administration [13]. Ultrasound has been demonstrated to be an excellent, rapid, safe, and cost-effective method of determining the size, amount, and location of fibroids [14]. During the menstrual cycle the endometrium undergoes cyclic changes in preparation for implantation. In the follicular phase, the growing follicles produce increasing amounts of estradiol that will induce proliferative endometrial changes [11]. Following ovulation, the corpus luteum produces progesterone that will initiate secretory changes. If implantation does not occur during the window of implantation, the endometrium will shed once the corpus luteum regresses [15]. A pelvic ultrasound an important part of clinical assessment. The use of transvaginal ultrasound to examine the endometrial cavity has revolutionized the examination of irregular uterine bleeding, allowing hysteroscopy to be reserved for patients who require removal of submucous fibroids or endometrial polyps [16]. Ultrasound may be used to fully describe adnexal masses in many cases, and for assessing congenital uterine malformations [17]. Endometrial disease is uncommon in premenopausal women who have abnormal uterine bleeding. Premenopausal women are said to have a 2% to 10% chance of developing endometrial hyperplasia [18]. Endometrial hyperplasia up to 3% to 23% of instances with complicated hyperplasia advance to endometrial cancer during a 13-year period [19]. Ultrasound is useful imaging modality to detect pathological and anatomical disorders effecting female body leading towards infertility. With the help of ultrasound we can measure endometrial thickness in different phases of menstrual cycle causing female infertility.

METHODS

In this descriptive study, 82 female patients with infertility were selected within fertile age group by convenient sampling at University Ultrasound Clinic, Lahore. Ultrasound machine of Toshiba xario 100 was used. Trans-abdominal and trans-vaginal scans were performed on these patients to measure endometrial thickness. Inclusive criteria were to have female patients of fertile age coming for infertility ultrasound examination. Patients with primary and secondary infertility in their secretory phase of menstrual cycle were considered for measuring endometrial thickness. Exclusive criteria were focused on fertile patients with pelvic abnormalities and female patients who have reached menopause. After the approval of synopsis, descriptive study was done at University Ultrasound clinic Lahore. Quantitative variables i.e. age, endometrial thickness, vintage was recorded on data collection sheets. All collected data was entered in SPSS (Statistical Package for Social Science) version 25.0. Analysis of data was done. The qualitative variables like type of infertility, day of mensuration were presented in form of frequencies and percentages (%). Mean and standard deviation was calculated for quantitative variables i.e. age, vintage, endometrial thickness. Qualitative data was represented by bar chart.

RESULTS

This was a study of total eighty-two patients ranging in age from 24 years to 46 years with average age of 32 years±4.8 years. The studied patients were of single gender, female. All the patients were studied for infertility and endometrial thickness was measured.

	Frequency	Percent
primary	45	54.9
secondary	37	45.1
Total	82	100.0

Table 1: Types of Infertility

Table 1 shows results that primary infertility is more in females than secondary infertility. There were 54.9% primary infertile those were not pregnant after one year of marriage. 45.1% secondary infertility, those get pregnant one time then were unable to conceive.

			type of infertility		
			primary	secondary	Total
Endometrial Thickness	9-12	Count%	10	11	21
		within ET	47.6%	52.4%	100.0%
	13-16	Count%	24	18	42
		within ET	57.1%	42.9%	100.0%
	17-20	Count%	11	5	16
		within ET	68.8%	31.3%	100.0%
	21-24	Count%	0	3	3
		within ET	0.0%	100.0%	100.0%
Total		Count%	45	37	82
		within ET	54.9%	45.1%	100.0%

Table 2: Endometrial Thickness with respect to type of infertility

Table 2 shows different endometrial thickness with respect to type of infertility in females. The results showed that primary infertility (54.9%) is more in females than secondary infertility (45.1%). There were 10(47.6%) females in primary infertility with 9-12mm endometrial thickness and 11(52.4%) in secondary infertility. 24(57.1%) females in primary infertility with 13-16mm endometrial thickness and 18(42.9%) in secondary infertility. 11(68.8%) females in primary infertility with 17-20mm endometrial thickness and 5(31.3%) in secondary infertility. 3(100%) females in secondary infertility with 21-24mm endometrial thickness and 0% in primary infertility.

The results showed primary infertility (54.9%) more in females than in secondary infertility (45.1). 4(100%) patients came for ultrasound on day 16 of their menstrual cycle 2(50%) with primary infertility and 2(50%) with secondary infertility. 19(100%) patients came on day 17 of their cycle 8(42.1%) with primary infertility and 11(57.1%) with secondary infertility. 14(100%) patients were present for scan on day 18, 8(57.1%) with primary infertility and 6(42.9%) with secondary infertility. 14(100%) patients were present for scan on day 19, 7(50%) with primary infertility and 7(50%) with secondary infertility. 2(100%) patients were present for scan on day 20, 1(50%) with primary infertility and 1(50%) with secondary infertility. 6(100%) patients were present for scan on day 21, 5(83.3%) with primary infertility and 1(16.7%) with secondary infertility. 6(100%) patients were present for scan on day 22, 4(66.7%) with primary infertility and 2(33.3%) with secondary infertility. 3(100%) patients were present for scan on day 23, 2(66.7%) with primary infertility and 1(33.3%) with secondary infertility. 3(100%) patients were present for scan on day 24, 1(33.3%) with primary infertility and 2(66.7%) with secondary infertility. 4(100%) patients were present for scan on day 26, 2(50%) with primary infertility and 2(50%) with secondary infertility. 3(100%) patients were present for scan on day 27, 1(33.3%) with primary infertility and 2(66.7%) with secondary infertility. 1(100%) patients were present for scan on day 28, 1(100%) with primary infertility. 3(100%) patients were present for scan on day 29, 3(100%) with primary infertility.

			Endometrial Thickness				
			9mm-12mm	13mm-16mm	17mm-20mm	21mm-24mm	Total
day of mensuration	16.00	Count%	3	1	0	0	4
		% within day of mensuration	75.0%	25.0%	0.0%	0.0%	100.0%
	17.00	Count%	11	8	0	0	19
		% within day of mensuration	57.9%	42.1%	0.0%	0.0%	100.0%
	18.00	Count%	5	7	2	0	14
		% within day of mensuration	35.7%	50.0%	14.3%	0.0%	100.0%
	19.00	Count%	2	10	2	0	14
		% within day of mensuration	14.3%	71.4%	14.3%	0.0%	100.0%
	20.00	Count%	0	2	0	0	2
		% within day of mensuration	0.0%	100.0%	0.0%	0.0%	100.0%
	21.00	Count%	0	4	2	0	6
		% within day of mensuration	0.0%	66.7%	33.3%	0.0%	100.0%
	22.00	Count%	0	2	4	0	6
		% within day of mensuration	0.0%	33.3%	66.7%	0.0%	100.0%
	23.00	Count%	0	2	1	0	3
		% within day of mensuration	0.0%	66.7%	33.3%	0.0%	100.0%
	24.00	Count%	0	1	1	1	3
		% within day of mensuration	0.0%	33.3%	33.3%	33.3%	100.0%
	26.00	Count%	0	0	3	1	4
		% within day of mensuration	0.0%	0.0%	75.0%	25.0%	100.0%
	27.00	Count%	0	1	1	1	3
		% within day of mensuration	0.0%	33.3%	33.3%	33.3%	100.0%
	28.00	Count%	0	1	0	0	1
		% within day of mensuration	0.0%	100.0%	0.0%	0.0%	100.0%
	29.00	Count%	0	3	0	0	3
		% within day of mensuration	0.0%	100.0%	0.0%	0.0%	100.0%
Total		Count%	21	42	16	3	82
		% within day of mensuration	25.6%	51.2%	19.5%	3.7%	100.0%

Table 4: Day of mensuration with respect to endometrial thickness day of mensuration * ET Crosstabulation

Table 4 shows day of mensuration with respect to endometrial thickness. At day 16 of cycle total 4(100%) patients 3(75%) 9-12mm, 1(25%) 13-16mm, endometrial thickness was present. At day 17 of cycle total 19(100%) patients 11(57.9%) 9-12mm, 8(42.1%) 13-16mm, endometrial thickness. At day 18 of cycle total 14(100%) patients 5(35.7%) 9-12mm, 7(50%) 13-16mm, 3(14.3%) 17-20mm endometrial thickness. At day 19 of cycle total 14(100%) patients 2(14.3%) 9-12mm, 10(71.4%) 13-16mm, 2(14.3%) 17-20mm, endometrial thickness. At day 20 of cycle total 2(100%) patients, 2(100%) 13-16mm, endometrial thickness. At day 21 of cycle total 6(100%) patients, 4(66.7%) 13-16mm, 2(33.3%) 17-20mm, endometrial thickness. At day 22 of cycle total 6(100%) patients, 2(33.3%) 13-16mm, 4(66.7%) 17-20mm, endometrial thickness. At day 23 of cycle total 3(100%) patients, 2(66.7%) 13-16mm, 1(33.3%) 17-20mm, endometrial thickness. At day 24 of cycle total 3(100%) patients, 1(33.3%) 13-16mm, 1(33.3%) 17-20mm, 1(33.3%) 21-24mm endometrial thickness. At day 26 of cycle total 4(100%) patients 3(75%) 17-20mm, 1(25%) 21-24mm endometrial thickness. At day 27 of cycle total 3(100%) patients, 1(33.3%) 13-16mm, 1(33.3%) 17-20mm, 1(33.3%) 21-24mm endometrial thickness. At day 28 of cycle total 1(100%) patients, 1(100%) 13-16mm, endometrial thickness. At day 29 of cycle total 3(100%) patient, 3(100%) 13-16mm, 21-24mm endometrial thickness.

Figure 1: shows that ETis measuring 15.5mm at 18th day of menstrual cycle. Patient's age was 30 years with primary infertility of 3 years

Figure 2: shows that ET is measuring 15.2mm at 20th day of menstrual cycle Patient's age was 34 years with secondary infertility of 7 years

DISCUSSION

Female infertility is highly affected by various factors including endometrial thickening. This is a study of 82 infertile patients, diagnosed using ultrasound. In this study out of 82 infertile females 45 (54.9%) patients had primary infertility and 37 (46.1%) had secondary infertility. Jason G. L. Bromer conducted a study in which he found that endometrial growing began from approximately 4.5 mm on cycle day 4, and is increased linearly to approximately 10 mm on cycle day 9. This same pattern was observed in all cycles, regardless of pregnancy or underlying diagnosis. Maximum endometrial thickness achieved showed a correlation with age, BMI, and maximum estradiol level. Subjects who carried a primary diagnose of PCOS, endometriosis, or RPL all achieved a significantly lower peak endometrial thickness than control subjects. There was a trend toward increased endometrial thickness in cycles resulting in pregnancy than those not. Diseases associated with infertility manifest a proliferative phase defect that can be recognized clinically [20]. Our study also shows that endometrial thickness was increased in secretory phase rather than in proliferative phase. Thickness continued to increase as days in menstrual cycle were increasing. P. Kovacs in his study states during the menstrual cycle the endometrium undergoes cyclic proliferative and secretory changes in preparation for implantation. He concluded that there were more follicles, oocytes and embryos as the endometrium was becoming thicker and the embryo quality was higher among women who became pregnant when compared with non-pregnant women after assisted reproduction. The pregnancy rate improved as endometrial thickness increased. No difference in cycle parameters and endometrial thickness was found between ongoing pregnancies and pregnancies that resulted in a first-trimester loss. Increased endometrial thickness is associated with higher pregnancy rates. In our study females who had thin endometrial lining in proliferative phase, had thickened endometrial lining during secretory phase and had the change of conceiving. At day 19 of their secretory phase 10 females had endometrial thickness between 13-16mm [13]. Ulla Larsen conducted a study in International Journal of Epidemiology on infertile women of Africa in which he found that infertility was more common among the women between ages 20-44. Women effected by primary infertility had age range of 20-29 years while women effected by secondary infertility had age range of 30-44 years. To avoid the challenges of distinguishing adolescent subfertility from infertility, the study began at the age of 20. Although the study stopped at the age of 44, the most of the surveys looked at included women aged 15 to 49 [21]. It is in concordance to our study that shows the age range of infertile female was 22-46 years. The mean age of women with primary infertility was 29±3 years and for secondary infertility were 36±3 years. Our study shows that most infertile women had endometrial hyperplasia present in (32.5%) of the total patients. Another study conducted by Valerie Beralin North America also showed that endometrial hyperplasia was most common among infertile women. 1750 couples were presented with infertility in the study. Abnormalities in endometrial lining were found to be in (31%) of the female patients. Tubal obstruction, endometriosis, luteal phase defects, and other ovulatory problems accounted for roughly a tenth of the diagnoses, while polycystic ovarian syndrome and cervical abnormalities each accounted for about 5%. Other diagnoses made up 12% of the remaining diagnoses, but no single cause was common enough to be evaluated separately. There was no clinical explanation for infertility in the remaining 10% of couples[22].

CONCLUSIONS

Female patients who initially taking infertility treatment had less endometrial thickness in proliferative phase; their

endometrial thickness maybe increased in early secretory phase or at 21st day of their menstrual cycle but they had lost their chance to conceive the pregnancy in proliferative phase due to less endometrial thickness. The females should know the normal endometrial thickness in different phases of their menstrual cycle to conceive the pregnancy. This study shows ultrasound plays a vital role in detecting endometrial thickness in infertility treatment.

REFERENCES

[1] Dreyer K, Van Rijswijk J, Mijatovic V, Goddijn M, Verhoeve HR, Van Rooij IA, et al. Oil-based or water-based contrast for hysterosalpingography in infertile women. 2017;376(21):2043-52. doi: 10.1056/NEJMoa1612337

[2] Johnson NPJA, Obstetrics NZJo, Gynaecology. Review of lipiodol treatment for infertility–an innovative treatment for endometriosis-related infertility? 2014;54(1):9-12. doi: 10.1111/ajo.12141

[3] Zhang B, Cui Y, Wang M, Li J, Jin L, Wu DJIA. In vitro fertilization (IVF) cumulative pregnancy rate prediction from basic patient characteristics. 2019;7:130460-7. doi: 10.1109/ACCESS.2019.2940588

[4] Nalaboff KM, Pellerito JS, Ben-Levi EJR. Imaging the endometrium: disease and normal variants. 2001;21(6):140924.doi.org/10.1148/radiographics.21.6.g01nv211409

[5] Sit AS, Modugno F, Hill LM, Martin J, Weissfeld JLJCE, Biomarkers P. Transvaginal ultrasound measurement of endometrial thickness as a biomarker for estrogen exposure. 2004;13(9):1459-65.

[6] Qiong Z, Jie H, Yonggang W, Bin X, Jing Z, Yanping LJF, et al. Clinical validation of pinopode as a marker of endometrial receptivity: a randomized controlled trial.2017;108(3):5137.e2.doi:10.1016/j.fertnstert.2017.07.006.

[7] Barker MA, Boehnlein LM, Kovacs P, Lindheim SRJJoar, genetics. Follicular and luteal phase endometrial thickness and echogenic pattern and pregnancy outcome in oocyte donation cycles. 2009;26(5):243-9. doi: 10.1007/s10815-009-9312-z.

[8] McWilliams GD, Frattarelli JLJF, sterility. Changes in measured endometrial thickness predict in vitro fertilization success. 2007;88(1):74-81. doi: 10.1016/j.fertnstert.2006.11.089.

[9] Gonen Y, Casper RF, Jacobson W, Blankier JJF, sterility. Endometrial thickness and growth during ovarian stimulation: a possible predictor of implantation in in vitro fertilization. 1989;52(3):446-50. doi: 10.1016/s0015-0282(16)60916-0.

[10] Sharara FI, Lim J, McClamrock HDJJoar, genetics. Endometrial pattern on the day of oocyte retrieval is more predictive of implantation success than the pattern or thickness on the day of hCG administration. 1999;16(10):523-8. doi: 10.1023/a:1020545120256.

[11] Dietterich C, Check JH, Choe JK, Nazari A, Lurie DJF, Sterility. Increased endometrial thickness on the day of human chorionic gonadotropin injection does not adversely affect pregnancy or implantation rates following in vitro fertilization–embryo transfer. 2002;77(4):781-6. doi: 10.1016/s0015-0282(01)03276-9.

[12] Rinaldi L, Lisi F, Floccari A, Lisi R, Pepe G, Fishel SJHr. Endometrial thickness as a predictor of pregnancy after in-vitro fertilization but not after intracytoplasmic sperm injection. 1996;11(7):1538-41.

[13] Kovacs P, Matyas S, Boda K, Kaali SJHR. The effect of endometrial thickness on IVF/ICSI outcome. 2003;18(11):2337-41. doi: 10.1093/humrep/deg461

[14] Wang L, Lv S, Mao W, Bai E, Yang XJBWsH. Fecundity disorders in older women: declines in follicular development and endometrial receptivity. 2020;20:1-8. doi.org/10.1186/s12905-020-00979-7

[15] Dickey RP, Olar T, Curole D, Taylor S, Rye PJHR. Endometrial pattern and thickness associated with pregnancy outcome after assisted reproduction technologies. 1992;7(3):418-21. doi: 10.1093/oxfordjournals.humrep.a137661

[16] Zeng F, Liang X, Chen ZJBI. New Roles for Clinicians in the Age of Artificial Intelligence. 2020;1(3):113-7. https://bio-integration.org/wp-content/uploads/2020/09/bioi20200014.pdf

[17] Goodfellow I, Bengio Y, Courville A. Deep learning: MIT press; 2016.https://www.deeplearningbook.org/

[18] Grande M, Borobio V, Jimenez JM, Bennasar M, Stergiotou I, Peñarrubia J, et al. Antral follicle count as a marker of ovarian biological age to reflect the background risk of fetal aneuploidy. Human Reproduction. 2014;29(6):1337-43. doi.org/10.1093/humrep/deu055

[19] Potočnik B, Zazula D, Korže D. Automated computer-assisted detection of follicles in ultrasound images of ovary. Journal of medical systems. 1997;21(6):445-57. doi: 10.1109/CBMS.1997.596402

[20] Bromer JG, Aldad TS, Taylor HSJF, sterility. Defining

the proliferative phase endometrial defect. 2009;91(3):698-704. doi: 10.1016/j.fertnstert.2007.12.066.

[21] Larsen UJljoe. Primary and secondary infertility in sub-Saharan Africa. 2000;29(2):285-91. doi: 10.1093/ije/29.2.285. PMID: 10817127.

[22] Beral V, Rolfs R, Joesoef MR, Aral S, Cramer DJJoE, Health C. Primary infertility: characteristics of women in North America according to pathological findings. 1994;48(6):576-9. doi: 10.1056/NEJMoa1612337