ENDOMETRIAL THICKNESS AND PREGNANCY OUTCOME IN IUI CYCLES

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ABSTRACT: OBJECTIVES: To investigate whether endometrial thickness on the day of hCG administration is a predictor of intrauterine insemination (IUI) success. **MATERIAL AND METHODS:** Three hundred and eighty women undergoing IUI cycles are analysed for Endometrial thickness on the day of hCG administration, Endometrial thickness measurement was done on the day of HCG administration. Correlation between endometrial thickness and factors such as age, dominant follicle numbers, stimulation protocols and pregnancy rate were assessed & compared between pregnant and non pregnant patients. A similar comparison was made between ongoing pregnancies and those that resulted in a loss in a University hospital-based infertility center from Dec 2011- Nov 2012. Main Outcome Measure(s): Endometrial thickness versus IUI outcome. **RESULTS:** In 220 couples, 365 cycles performed. Pregnancy rate was 14.5%. 90% of pregnancies were ongoing. The mean age of females was 28.6 & mean ET was 8.1mm $\pm$ 1.47. The mean ET in age range 17-25 yrs was 7.4 $\pm$ 1.98 mm and in age range of >40 years was 6.9 $\pm$ 1.7 mm ($p=0<001$ HS). With increasing the number of 16-18 mm follicles pregnancy rate was 16%, 11% & 15.6% with 1, 2 & >3 follicles. No statistically significant correlation was found between the two.

INTRODUCTION: To obtain a higher likelihood of achieving pregnancy, IUI is usually synchronized with ovulation, either in a natural or a stimulated cycle. The overall success of IUI varies, with pregnancy rates between 5 and 26% per cycle (1). During ovulatory cycles, pattern and thickness of endometrial is variable. After menstruation, endometrium is thin and becomes thicker gradually. Although many studies were done about affecting factors on endometrial thickness in infertile women, over the years, but the results is still unclear (2,3). The aim of this study was to determine the effect of some factors such as age, number of follicles on the endometrial thickness and its impact on pregnancy in intrauterine insemination cycles.

OBJECTIVE: To discover the factors contributing to endometrial thickness, and to assess the impact of endometrial thickness on pregnancy rates (PRs) according to these factors.

MATERIAL & METHODS: In this study we have evaluated a total of 365 IUI cycles at SMS Medical College Jaipur (Dec 2011 to Nov 2012 infertile women considered for intrauterine insemination (IUI). Endometrial thickness measurement was done on the day of HCG administration. Cycles were natural/stimulated with letrozole 5 clomiphene citrate and/or gonadotrophins (HMG/FSH). Letroz 50-100 mg clomiphene citrate (D3-D7), followed by 75-150 IU of gonadotrophins added. Correlation between endometrial thickness and factors such as age, total follicle number and pregnancy rate were assessed. Ovarian (Follicle maturation) and endometrial responses monitored by serial TVS D9-13. 5000-10000 IU HCG administered (when at least one follicle mean diameter was >18 mm. On the day of hCG administration, TVS scan measure endometrial thickness &

ORIGINAL ARTICLE

Measurements made from the outer edge of the endometrial-myometrial interface to the outer edge in the widest part of the endometrium. In this study, we evaluated endometrial thickness within 3 ranges of ≤ 6 , $6 < ET \leq 10$ and > 10 mm. IUI was performed 36 h after administration of HCG. Women remained supine for 10–15 min after IUI. Luteal phase was supported by daily vaginal administration of 200 mg progesterone b.d. for 14 days. Plasma β -hCG levels were measured routinely, 2 weeks after IUI. Clinical pregnancy was defined as TVS visualization of intrauterine gestational sac(s).

Statistical analysis: Quantitative data-sum up in mean plus SD, the difference in means of different groups was analysed using ANOVA. Qualitative data- sum up in proportions, difference in % using chi square test Data was analyzed with SPSS software and bivariate and multivariate analysis was done, to predict infertility using endometrial thickness and other patients parameter like age, Logistic regression analysis was performed too. Results were considered statistically significant for $P < 0.05$.

RESULT: In 220 couples, 365 cycles performed. Their base line demographics are shown in **Table 1**. Pregnancy rate was 14.5%, of these 90% of pregnancies were ongoing. The pregnancy rate was 27.5% when the endometrial thickness was between 6 to 10 mm. **Table 2**.

Age in years	No. of cycles % (n)	Clinical Pregnancy % (n)	Ongoing % (n)	Missed % (n)
17-25	86	16.2(14)	12.7(11)	3
26-35	255	14.3(38)	12.8(35)	2
35-40	23	8.6(2)	8.6(2)	0
>40	1	0	0	0
Causes of infertility				
Male factor	19.7(72)	20.8(15)	20.8(15)	0
PCOS	22.7(83)	24.7(20)	20.4(17)	3
ENDOMETRIOSIS	4.6(17)	5.8(1)	0	1
UNEXPLAINED	47.6(174)	9.7(17)	9.1(16)	1
M+PCOS	5.2(19)	26.3(5)	26.3(5)	0
Duration of infertility (yrs)				
≤ 6	57(208)	16.8(35)	31	4
>6	43(157)	10.8(17)	16	1
Type				
P	294	13.6(40)	12.5(37)	3
S	71	16.9(12)	14(10)	2
Total sperm count				
$\geq 5-15$	8	0	0	0
>15-30	36	5.5(2)	0	2
>30-45	30	16.6(5)	13.3(4)	1
>45	224	12.9(30)	12.5(28)	2
	268	13.8(37)	12(32)	
azoo	67	22.3(15)	22.3(15)	0

ORIGINAL ARTICLE

Motile fraction				
<40%	45	7	6	1
>=40%	247	30	26	4

Table1: Base line demographics

ET	NO. OF CASES (n=)	NO.OF PREGNANCIES (n=)	%
<6	17	2	11.7
6-<8	140	12	8.5
8-<10	173	33	19
10-<12	23	3	13
>=12	12	3	25
TOTAL	365	53	14.5

Table 2: Endometrial thickness & pregnancies achieved

The means age of patients was 28.69 ± 4 years and 93.4% of them were ≤ 35 years of age (Table 3). The mean endometrial thickness was 8.12 ± 1.47 mm (range, 4-14 mm).

In 4.79% of patients endometrial thickness (ET) was ≤ 6 mm and in 87.85% it was $6 < ET \leq 10$ mm and in 7.35% it was > 10 mm (Table 3). Pregnancy rate was 16.6%. Table 3) presents pregnancy rates according to ET and patients age. Pregnancy rate in patients < 35 years old with $ET \leq 6$ mm was 14.29% and with $6 < ET \leq 10$ mm was 15.44%, this difference was statistically not significant ($p < 0.05$). Pregnancy rate in patients > 35 years $ET \leq 6$ mm was 0% and with $6 < ET \leq 10$ mm was 37.5%, ($p < 0.05$). Pregnancy rate in all age ranges with $ET \leq 6$ mm, $6 < ET \leq 10$ mm and $ET > 10$ mm was 13.33%, 16.73% and 17.39% respectively ($p > 0.05$ ns). Effects of some factors such as age, and follicle number on ET were studied.

In older patients, mean ET was lower (Table 4). For example, mean ET in age range of 17-25 years was 8.14 ± 1.58 mm and in age range of > 40 years was 7.5 ± 0 mm ($p = 0.001$ HS). With increasing the number of 16-18 mm follicles (≥ 4) endometrium was thicker but no statistical significance was considered too. . A logistic regression analysis (Table 5) executed for parameters that correlated with $ET \leq 6$ mm. We found that > 25 years old patients had an OR for developing a thin endometrium, compared to < 25 years old patients, with an OR of 0.264 There was a meaningful p-value for odd ratios, in all of parameters.

Pregnancy/age (years)	Total	$1 \geq ET \geq 6$ mm	$6 < ET \leq 10$ mm	$ET > 10$ mm	p-value
	no (%)	no (%)	no (%)	no (%)	
≤ 35	295	14(4.76%)	259(87.80%)	22(7.46%)	
Pregnancy + age ≤ 35	46	2(14.29%)	40(15.44%)	4(18.18%)	0.953NS
> 35	18	1(5.55%)	16(88.89%)	1(5.55%)	
Pregnancy + age > 35	6	0	6(37.5%)		0.048 S
All age ranges	313	15(4.79%)	275(87.85%)	23(7.35%)	

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Pregnancy in all ages	52	2(3.85%)	46(88.46%)	4(7.70%)	0.954 NS
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Table 3: Association between pregnancy rate with age and ET.

Parameters	Total	1≥ ET≥ 6 mm	6 < ET ≤ 10 mm	ET>10 mm	Mean ET (mm)	p-value
	no (%)	no (%)	no (%)	no (%)		
Age Groups						
17-25	86	12(14%)	63(73.3%)	11(12.8%)	8.14+ _{-1.58}	
26-35	255	4(1.6%)	236(92.5%)	15(5.9%)	8.11+ _{-1.36}	<0.001HS
36-40	23	1(4.3%)	21(91.3%)	1(4.3%)	8.13+ _{-2.21}	
>40	1	0	1(100%)	0	7.50	
Follicle number (16-18mm)						
1	212	11(5.2%)	184(86.8%)	17(8%)	8.18+ _{-1.52}	
2 to 3	140	6(4.3%)	125(89.3%)	9(6.4%)	8.01+ _{-1.41}	0.0886NS
4 to 5	13	0	12(92.3%)	1(7.7%)	8.34+ _{-1.23}	
>6	0					

Table 4: Affecting factors on ET

	OR	95% confidence Interval	p value
Year			
17-25	0.267	0.50-1.429	0.123
>25			

Table 5: Logistic regression model for ET ≤6 mm

DISCUSSIONS: Correlation between ET and pattern with pregnancy rate and predisposing factors for growth of endometrium are unclear. In this study, we evaluated endometrial thickness within 3 ranges of ≤6, 6<ET≤10 and >10 mm. Habibzadeh et al concluded Pregnancy rate in patients <35 years old with ET≤6 mm was 8% and with 6<ET≤10 mm was 16.2%, Pregnancy rate in patients > 35 years old with ET ≤6 mm was 3.1% and with 6<ET≤10 mm was 10%, Pregnancy rate in all age ranges with ET≤6 mm and 6<ET≤10 mm was 8.9% and 15.6% respectively. Pregnancy rate in all age ranges in ET>10 mm was zero (4). In our research, pregnancy rate was studied, in age ranges (<35yrs and 35< years) with different endometrial thickness (≤6, 6<ET≤10 and >10 mm).In all age ranges; pregnancy rate was lower with ET≤6 mm. & >35yrs. Reuter et al concluded that endometrial thickness of at least 8 mm, with a high number of follicles (up to three) with an average of 15 mm are correlated with a higher rate of conception (5). Gonen et al 1990 who reported poor PR with endometrial thickness < 6 mm (6). However in our study (Table 2) Pregnancy rate in ET< 6mm was 11%.We did not find a correlation between number of follicles with ET. This study also showed that the number of dominant follicle were not significantly associated with pregnancy outcome. S. Moradan study indicated that the pregnancy rate in IUI method has a significant relation with

endometrial thickness equal or more than 7 mm, but there is no such relationship with equal or more than 3 dominant follicle. Kolibianakis studied main outcome measure ongoing pregnancy. No difference was observed in endometrial thickness between patients who did or did not achieve an ongoing pregnancy (7.6 +/- 0.3 versus 7.6 +/- 0.2 respectively; P = 0.7). (8)

Rashidi did not report any difference in terms of endometrial thickness and pattern between pregnancy positive and pregnancy negative patients (9). Esmailzadeh et al reported Mean (SD) endometrial thickness on the day of hCG administration was significantly greater in cycles where pregnancy was achieved. (10.1 +/-3.0 vs. 7.7+- 3.5). They reported pregnancy rates were related to the woman's age, suggesting that aging effects may begin after 30 years. (10).

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1191 cycles in which the endometrial thickness was equal to or more than 6 mm and resulted in 183 (15.4%) positive BHCGs and 165(13.6%) normal early pregnancy ultrasounds were compared to 246 cycles in which the endometrial thickness was less than 6 mm resulted in 19 (7.7%) positive BHCGs and 11 (4.5%) normal early pregnancy ultrasounds. The difference was statistically significant using a chi-squared test.

CONCLUSION: The results of the present study identified a statistically significant difference in mean endometrial thickness between cycles that resulted in pregnancy and those that did not. This study showed that the number of dominant follicle were not significantly associated with pregnancy outcome. In all age ranges, chance of pregnancy is higher with endometrial thickness of $6 < ET \leq 10$ mm.

Fig. 1:

Fig 2:

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