

Title: IS THICKER BETTER? ENDOMETRIAL THICKNESS AT THE TIME OF INTRAUTERINE INSEMINATION

Authors: Shelley Dolitsky¹, Peter Lindner¹, Elizabeth Clain², Joshua Morris³, Laura Zalles⁴, Selena Park¹, Jerry Wang⁵, Samad Jahandideh⁴, Kerry Flannagan⁴, Alan DeCherney¹, Micah Hill^{1,6}, Kate Devine^{1,7}, Phillip Romanski⁵, Matthew Connell⁴

¹ Department of Reproductive Endocrinology and Infertility, National Institutes of Health, Bethesda, MD

² Department of Reproductive Endocrinology and Infertility, University of Colorado, Aurora, CO

³ Department of Reproductive Endocrinology and Infertility, Eastern Virginia Medical School, Norfolk, VA

⁴ Shady Grove Fertility, Rockville, MD

⁵ Shady Grove Fertility, New York, NY

⁶ Department of Reproductive Endocrinology and Infertility, Walter Reed National Military Medical Center, Bethesda, MD

⁷ Shady Grove Fertility, Washington, DC

Background: Current data regarding the association between endometrial thickness during intrauterine insemination (IUI) cycles and clinical pregnancy report conflicting results. Published studies primarily analyze various arbitrary endometrial thickness thresholds, did not report the appearance of the lining, and are limited by sample size (1-4).

Objective: The objective was to investigate the association between endometrial thickness at the time of trigger during IUI cycles and pregnancy. We tested the hypothesis that in patients with a trilaminar endometrial lining, endometrial thickness at the time of trigger is associated with pregnancy.

Materials and Methods: This retrospective cohort study included patients age 18-50 years who underwent IUI between 2010 and 2023 at US Fertility practices. The primary outcome was pregnancy, defined as a patient with a positive beta hCG measured with a blood test 14 days after IUI. The secondary outcome was ongoing pregnancy, defined as patients with clinical intrauterine pregnancies that were discharged from US Fertility between 8- and 10-weeks gestation. Only medicated cycles using ovulation induction medication were included. Patients were excluded if they did not have a trilaminar appearing endometrial lining, had severe oligospermia (total motile count ≤ 5 million), or had uterine factor infertility. Endometrial thickness was analyzed as a continuous variable. Primary analysis was performed including all patients undergoing ovulation induction and IUI cycles. Secondary analysis was performed stratifying patients by ovulation induction medication used. We estimated risk ratios (RR) and 95% confidence intervals (CI) using modified Poisson regression models fitted with generalized estimating equations to account for correlation among cycles from the same patient. P values were from Wald tests of the model parameters.

Result(s): A total of 19,138 patients were included in the analysis. The average age of the patients was 34.2. Most patients had unexplained infertility (31.4%), ovulatory disorders (21.2%), diminished ovarian reserve (13.4%), or male infertility (12.9%). Patients averaged 1.95 (+/- 1.08) follicles ≥ 14 mm on the day of trigger. For all patients undergoing ovulation induction and IUI cycles, for every 1mm increase in thickness of the endometrial lining, there was a 2% higher likelihood of pregnancy (95% CI: 1%-4%, $p=0.0006$) and a 3% higher likelihood of

ongoing pregnancy (95% CI: 2%-5%, $p < 0.0001$) (Table 1). These results were similar in the patients undergoing ovulation induction with clomiphene citrate (Table 2). However, when analyzing patients taking letrozole or gonadotropins for their ovulation induction/IUI cycles, this improvement in pregnancy outcomes was not seen (Table 2).

Conclusion(s): In patients with a trilaminar endometrial lining, the endometrial thickness at the time of trigger in patients proceeding with IUI was weakly associated with pregnancy. However, the marginal increase in pregnancy observed with each 1mm of increase in endometrial thickness is not clinically meaningful and therefore IUI cycles with a trilaminar lining should not be cancelled based on a thin endometrium alone.

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Table 1: Comparison of pregnancy outcomes for all IUI cycles based on endometrial thickness.

Cycle outcome	n = 19138	aRR per 1mm endometrial thickness (95% CI) p-value
Pregnancy	3364 (17.6%)	1.02 (1.01, 1.04); P=0.0006
Ongoing pregnancy	2617 (13.7%)	1.02 (1.02, 1.05); P<0.0001

Results shown as n (%). IUI = intrauterine insemination; aOR = adjusted odds ratio; CI = confidence interval.

Table 2: Comparison of endometrial thickness and pregnancy outcomes for each ovulation induction medication used

Cycle outcome		aRR per 1mm endometrial thickness (95% CI) p-value
Clomiphene Citrate	n =9533	
Pregnancy	1581 (16.6%)	1.03 (1.01, 1.05); P<0.0001
Ongoing pregnancy	1202 (12.6%)	1.04 (1.01, 1.06); P<0.0001
Letrozole	n=5846	
Pregnancy	1059 (18.1%)	1.00 (0.98, 1.03); P=0.78
Ongoing pregnancy	851 (14.6%)	1.01 (0.98, 1.04); P=0.64
Gonadotropins	n=3759	
Pregnancy	724 (19.3%)	1.01 (0.98, 1.05); P=0.35
Ongoing pregnancy	564 (15.0%)	1.02 (0.99, 1.06); P=0.17

Results shown as n (%). IUI = intrauterine insemination; aOR = adjusted odds ratio; CI = confidence interval.