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Title:

DOES THE NUMBER OF MATURE FOLLICLES IN OVULATION INDUCTION CYCLES AT THE TIME OF TRIGGER CORRELATE WITH MULTIPLE GESTATION RATE?

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Background:

Ovulation induction (OI) cycles with oral medications such as clomiphene citrate and letrozole are common first line treatments for infertile patients. Striking a balance between over and under-stimulation during OI is essential in preventing multiple gestations while increasing chances of achieving a single, healthy pregnancy.

Objective:

This study sought to evaluate whether the number of mature follicles at the time of trigger in OI cycles with oral medications is correlated with the rate of multiple gestations.

Materials and Methods:

In this retrospective cohort study, patients who underwent OI using CC or letrozole followed by an intrauterine insemination from 2002-2017 were included. Patient and partner age, BMI, ovarian reserve testing, endometrial thickness at the time of trigger, gravidity, parity, and sperm source were recorded. Clinical pregnancy (CP) was confirmed by the presence of fetal cardiac



activity on ultrasound. Data was analyzed using a student's t-test, chi-squared and binary logistic regression model.

Results:

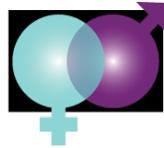
A total of 11,722 OI cycles were performed. There was no difference in patient age, BMI or ovarian reserve outcome between patients who had a multiple or singleton gestation. While not statistically significant, there was a trend toward a higher AMH level among patients who had a multiple gestation compared with those with singletons (5.88 vs 3.66, $p=0.08$). Multiple gestation rate did not differ among patients taking CC or letrozole (0.79% vs 0.6%, $p=0.31$). Likelihood of CP and ongoing pregnancy (OP) was higher among patients who had more mature follicles. When two or more follicles were present at the time of trigger, OP rates increased twofold (OR 2.34, 95% CI 1.40-3.90) and when there were three or more follicles, pregnancy rates increased threefold (OR 3.38, 95% CI 1.95-5.86). While there were significantly more mature follicles in patients who had a multiple gestation as compared with singleton (2.32 vs 1.93, $p<0.001$), after controlling for age, parity, and ovarian reserve markers, there was no difference in likelihood of multiple gestation based on the number of follicles present (2 follicles OR 2.74, 95% CI 0.79-9.47, ≥ 3 follicles OR 2.31, 95% CI 0.63-8.46).

Conclusions:

While the presence of more than one mature follicle increases the likelihood of achieving an OP, additional mature follicles does not boost the rate of multiple gestations. Given the risks associated with multiple gestations, these results are particularly reassuring in the management of younger patients undergoing OI who have multi-follicular development.

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Table 1:

	Multiple Gestation (n=87)	Singleton Gestation (n=880)	P Value
Age (y)	33.9 ± 4.12	34.5 ± 3.98	NS
BMI (kg/m ²)	25.1 ± 6.14	24.4 ± 4.69	NS
Day 3 FSH (IU/mL)	7.71 ± 3.36	7.00 ± 2.42	0.08
Day 3 Estradiol (pg/mL)	53.6 ± 25.0	48.2 ± 18.9	0.08
Anti-mullerian Hormone (pmol/L)	5.88 ± 5.60	3.66 ± 3.99	0.08
Endometrial Thickness at time of trigger (mm)	8.75 ± 1.59	8.74 ± 1.51	NS
Previous number of Ovulation Induction cycles	2.38 ± 2.18	2.26 ± 1.98	NS
Gravidity	0.79 ± 1.08	1.29 ± 1.23	0.004
Parity	0.34 ± 0.60	0.64 ± 0.74	0.003
Partner Age	36.3 ± 4.56	36.6 ± 5.58	NS
Donor Sperm Source	12.7% (11/87)	8.5% (75/880)	NS
Total Number Follicles > 18mm	2.32 ± 1.02	1.93 ± 0.94	<0.001

Table 2:

	Clomiphene Citrate	Letrozole	P Value
Clinical Pregnancy Rate	9.1% (806/8899)	9.6% (272/2823)	NS
Ongoing Pregnancy Rate	8.1% (723/8899)	8.6% (244/2823)	NS
Multiple Pregnancy Rate	0.79% (70/8899)	0.60% (17/2823)	NS