

Total Motile Sperm Count and Oral Ovulation Induction Protocols are not Predictors of Success in Donor Insemination Cycles: Results from a Large Retrospective Cohort Study.

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WHAT IS KNOWN ALREADY

There are inconsistent results regarding the effect of sperm parameters on success rates of artificial insemination with donor (AID). Besides, the need for ovulation induction and for hCG trigger in this category of patients is questionable, and its effectiveness over natural cycles is not yet confirmed in the literature, despite being a common practice.

STUDY PURPOSE

To investigate the effect of TMS count and ovulation induction on clinical pregnancy rate in AID cycles.

STUDY DESIGN, SIZE, DURATION

Patients who underwent AID cycles at the university-affiliated fertility center-OVO clinic in Montreal, Canada between 2011 and 2015 were retrospectively selected. A total of 4333 AID cycles were performed on 1179 patients, resulting in 744 pregnancies.

Demographic Characteristics	All patients N= 4333 mean± Sd median (IQR range)	Clinical pregnancy N= 487 mean± Sd median (IQR range)	No clinical pregnancy N= 3846 mean± Sd median (IQR range)
Age (years)	34.88 ±4.83	33.63 ±4.736	35.04 ±4.82
BMI (Kg/m ²)	26.9 ± 6.2	27.47 ± 6.18	26.84 ± 6.24
AMH (ng/ml)	1.9 (2.61)	1.88 (2.48)	1.9 (2.62)
Menstrual cycle (days)	29 ± 4.56	29.64 ± 5.44	28.956 ± 4.43
Endometrial thickness (mm)	8.16 ± 2.21	8.41 ± 3.36	8.12 ± 2
Follicles ≥14 mm	1.69 ± 0.98	1.78 ± 1	1.68 ± 0.97
Previous IUI	2.97 ± 3.018	3.01 ± 3.107	2.97 ± 3
Previous failed AID	2.73 ± 2.82	2.67 ± 2.84	2.73 ± 2.81
Previous successful AID	0.23 ± 0.538	0.32 ± 0.577	0.22 ± 0.532
Indication			
Single patient	1681 (38.8%)	143 (29.4%)	1538 (40.0%)
Homosexual female couple	1779 (41.1%)	230 (47.2%)	1549 (40.3%)
Male factor	868 (20.0%)	113 (23.2%)	755 (19.6%)
Smoking status			
Smoker	359 (8.3%)	41 (8.4%)	318 (8.3%)
Non-smoker	3856 (89%)	427 (87.7%)	3429 (89.2%)

Table 1. Demographic Characteristics of Included Patients

INCLUSION CRITERIA

- AID cycle

EXCLUSION CRITERIA

- Uterine factor infertility
- Tubal factor infertility
- Recurrent pregnancy losses
- Abnormal hormonal profile (TSH, Prolactin)

PRIMARY OBJECTIVE

- Clinical pregnancy rate

SECONDARY OBJECTIVES

- Positive B-hCG rate
- Multiple pregnancy rate
- Miscarriage rate

PARTICIPANTS/MATERIALS, SETTING, METHODS

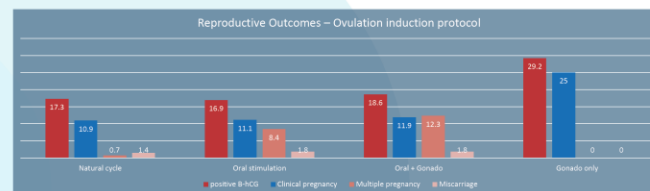
Cycles were divided into 8 groups based on TMS count (in million): <0.5, [0.5-1], [1-5], [5-10], [10-20], [20-40], [40-80], and ≥80. A TMS of 10 to 20 million was selected as a reference level. Ovulation induction was divided into oral stimulation, combined oral and gonadotropin stimulation and gonadotropin-only stimulation, and compared to natural cycles. The use of hCG ovulation trigger was also compared to urinary ovulation monitoring. Regression analysis was performed using patient demographic and cycle characteristics.

Cycle Characteristics	All patients	Clinical pregnancy N= 487	No clinical pregnancy N= 3846
Protocol			
Natural	1298 (30.0)	142 (29.2%)	1156 (30.1%)
Oral	2464 (56.9%)	274 (56.3%)	2190 (56.9%)
Oral + Gonadotropin	547 (12.6%)	65 (13.3%)	482 (12.5%)
Gonadotropin only	24 (0.6%)	6 (1.2%)	18 (0.5%)
hCG trigger			
Yes	786 (18.1%)	408 (83.8%)	3134 (81.5%)
No	3542 (81.7%)	78 (16.0%)	708 (18.4%)
Total Motile sperm (TMS) count (million)			
<0.5	8 (0.2%)	1 (0.2%)	7 (0.2%)
[0.5-1]	28 (0.6%)	2 (0.4%)	26 (0.7%)
[1-5]	625 (14.4%)	79 (16.2%)	546 (14.2%)
[5-10]	530 (12.2%)	58 (11.9%)	472 (12.3%)
[10-20]	1234 (28.5%)	123 (25.3%)	1111 (28.9%)
[20-40]	1502 (34.7%)	174 (35.7%)	1328 (34.5%)
[40-80]	389 (9%)	48 (9.9%)	341 (8.9%)
≥80	17 (0.4%)	2 (0.4%)	15 (0.4%)

Table 2. AID Cycle Characteristics

MAIN RESULTS AND THE ROLE OF CHANCE

There was no significant difference in positive β-hCG result, clinical pregnancy, multiple pregnancy and miscarriage rates when comparing all ranges of TMS count to a reference of 10 to 20 million. When dividing patients based on the protocol for ovulation induction, clinical pregnancy rate was significantly higher in the gonadotropin-only stimulation group (OR 4.116, [1.379, 12.287]) but not in other types of stimulation, as compared to natural cycles. hCG triggering resulted in a similar clinical pregnancy and miscarriage rates, but a higher multiple pregnancy rate when compared to urinary LH testing (7.7% versus 1.3%, p=0.045). A multivariate logistic regression analysis for predictors of clinical pregnancy accounting for relevant demographic and cycle characteristics was conducted. No significant difference was noted in different ranges of TMS and the groups of ovulation induction. In this model, age was found to be a significant predictor. In particular, with every one-year increase in age, the odds of clinical pregnancy decrease by 6.4% (Adjusted OR 0.936; 95%CI [0.914, 0.958]).

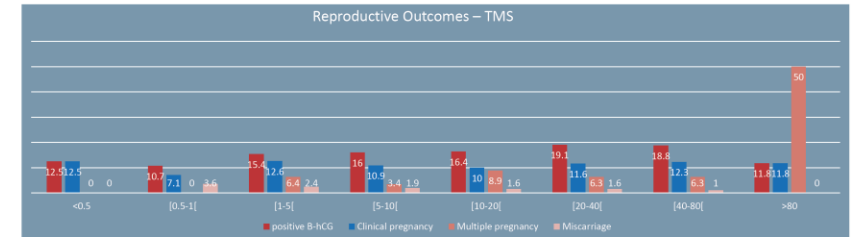


	Natural	Oral	Oral + Gn	Gn only	P value (all groups together)
Positive B-hCG rate	224/1298 (17.3%)	416/2464 (16.9%)	102/547 (18.6%)	7/24 (29.2%)	<0.001
Clinical pregnancy rate	142/1298 (10.9%)	274/2464 (11.1%)	65/547 (11.9%)	6/24 (25%)	0.196
Multiple pregnancy rate	1/142 (0.7%)	23/274 (8.4%)	9/65 (12.3%)	0	<0.001
Miscarriage rate	18/1298 (1.4%)	45/2464 (1.8%)	10/547 (1.8%)	0	0.842

Table 3. Reproductive Outcomes by Ovulation Induction Protocols

DISCUSSION

Our results are consistent with many studies in the literature regarding the effect of TMS and ovulation induction protocols on the reproductive outcomes in IUI cycles. It is reasonable, based on our findings, to consider decreasing the burden of medication and to accept lower levels of TMS in AID cycles.



	<0.5	[0.5-1]	[1-5]	[5-10]	[10-20]	[20-40]	[40-80]	≥80
Positive B-hCG rate	1/8 (12.5%)	3/28 (10.7%)	96/625 (15.4%)	85/530 (16.0%)	202/1234 (16.4%)	287/1502 (19.1%)	73/389 (18.8%)	2/17 (11.8%)
Clinical pregnancy rate	1/8 (12.5%)	2/28 (7.1%)	79/625 (12.6%)	58/530 (10.9%)	123/1234 (10%)	174/1502 (11.6%)	48/389 (12.3%)	2/17 (11.8%)
Multiple pregnancy rate	0	0	5/79 (6.4%)	2/58 (3.4%)	11/123 (8.9%)	11/175 (6.3%)	3/48 (6.3%)	1/2 (50%)
Miscarriage rate	0	1/28 (3.6%)	15/625 (2.4%)	10/530 (1.9%)	20/1234 (1.6%)	23/1502 (1.6%)	4/389 (1.0%)	0

Table 4. Reproductive Outcomes by TMS Group

LIMITATIONS, REASONS FOR CAUTION

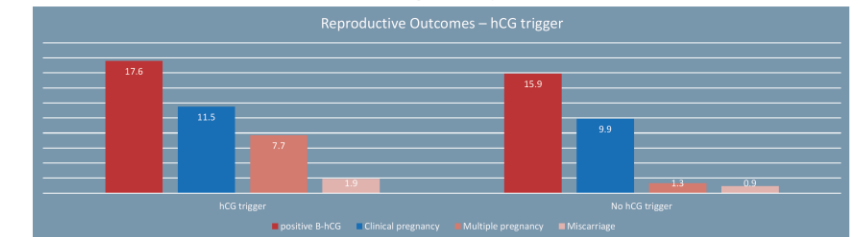
In our study, cycles with TMS count below 1 million are limited. Thus, results should be viewed with caution in this group, without cycle cancellation, since clinical pregnancy can be achieved. Moreover, our results cannot be generalized on infertile couples given the characteristics of our population of interest.

WIDER IMPLICATIONS OF THE FINDINGS

Minimal or maximal cut-off values for TMS in AID cycles should not be used as indicators for cycle cancellation. Natural cycles are as successful as oral ovulation induction. hCG trigger, unless indicated, should not be used as it is associated with higher risk of multiple pregnancy without increasing clinical pregnancy.

	Crude OR	Adjusted OR
Age	0.943; 95%CI: 0.922, 0.965 (P<0.01)	0.936; 95%CI: 0.914, 0.958 (P<0.001)
hCG trigger status		
No	Reference	Reference
Yes	1.255; 95%CI: 0.924, 1.704 (P=0.145)	1.197; 95%CI: 0.843, 1.699 (P=0.314)
Protocol		
Natural	Reference	Reference
Oral	1.120; 95%CI: 0.868, 1.444 (P=0.384)	1.162 (0.869, 1.554) P=0.310
Oral + Gn	1.091 (0.753, 1.582) P=0.645	1.312 (0.871, 1.977) P=0.194
Gn only	4.116; 95%CI: 1.379, 12.287 (P=0.011)	5.461; 95%CI: 1.779, 16.764 (P=0.003)
TMS		
[10-20]	Reference	Reference
<0.5	0 P: 0.999	0 P: 0.999
[0.5-1]	0.846 (0.195, 3.67) P=0.846	0.821 (0.188, 3.584) P=0.793
[1-5]	1.327 (0.781, 1.684) P=0.114	1.272 (0.891, 1.816) P=0.185
[5-10]	1.147 (0.781, 1.683) P=0.484	1.160 (0.788, 1.709) P=0.451
[20-40]	1.258 (0.945, 1.672) P=0.116	1.271 (0.951, 1.698) P=0.105
[40-80]	1.281 (0.832, 1.97) P=0.260	1.341 (0.868, 2.070) P=0.186
≥80	1.481 (0.326, 6.725) P=0.611	1.845 (0.402, 8.457) P=0.431

Table 6. Regression Analysis Outcomes



	hCG trigger	No hCG trigger	P value
Positive B-hCG rate	623/3542 (17.6%)	125/786 (15.9%)	0.274
Clinical pregnancy rate	408/3542 (11.5%)	78/786 (9.9%)	0.212
Multiple pregnancy rate	32/408 (7.7%)	1/78 (1.3%)	0.045
Miscarriage rate	66/2542 (1.9%)	7/786 (0.9%)	0.138

Table 5. Reproductive Outcomes by hCG Trigger Group