

## Pregnancy loss after implantation in IVF. Searching for clues.

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**Objectives:** To identify the factors that predicts pregnancy loss in IVF after confirmed implantation with positive HCG.

**Design:** Multivariate logistic regression analysis of clinical data collected prospectively.

**Setting:** Private fertility centre

### Materials and methods

The patients undergoing IVF, ICSI and frozen embryo transfers from Apr. 2007 to Dec. 2008 were included in the analysis.

All patients with  $\beta$ -HCG above 10 mmol/L were considered to have had implantation after embryo transfer. Only patients under the age of 40 years were included to minimize the age effect. Transfers were done on day 3, 4 or 5. Stimulation protocols for IVF were either the long agonist protocol or the short antagonist protocol, decision on which protocol was decided by the treating physician.

Frozen embryo transfers were done mostly in natural cycles with estradiol supplementation if ovulation was not evident. Oocyte retrievals were performed 36 hours after HCG injection. Recovered oocytes were fertilized with ICSI or insemination depending on the parameters of sperm analysis. The embryos were cultured with sequential media in 5% O<sub>2</sub>, 6% CO<sub>2</sub> at 37 °C .

Good quality embryos on day 3 or day 5 were selected for intrauterine transfer under ultrasound guidance. Pregnancy was detected by measuring HCG at day 12 (day 3 ET) or day 10 (day 5 ET) following embryo transfers and clinical pregnancy was confirmed by fetal heart beats detected by ultrasound at 7weeks of gestation. A number of variables (listed in the table) were included for means comparison (students' test) and percentage comparison ( $\chi^2$  test).

Variables that are found to be significant in the paired test were included in the logistic regression model as independent variables; pregnancy loss or viable pregnancy are considered dependant variables. A total of 241 cycles with initial  $\beta$ -HCG positives were subjected to the analysis.

### Results:

From Apr., 2007 to Dec., 2008, the fresh cycle outcomes of pregnancies are 66.0% (HCG positive, 241/360), 51.6% (Viable Pregnancy, 186/360); the FET cycle outcomes of pregnancies are 60.9% (HCG positive, 118/194), 44.3% (Viable Pregnancy, 86/194). The factors affecting chemical vs. gestational pregnancies are listed in the following table.

Variables	Chemical preg. Mean, STD, n	HB Mean, STD, n	%	P values	Scores from logistic regression
<b>HCG*</b>	63.51±8.5, 55	444±58.6, 186		0.0004	<b>49.44</b>
<b>Total dose of FSH*</b>	2552±161.4, 55	2077±78, 186		0.006	

					<b>8.56</b>
<b>Age*</b>	33.78±0.6, 55	32.44±0.3, 186		0.03	<b>5.58</b>
<b>Day 3 FSH*</b>	6.213±0.34, 55	5.44±0.2, 186		0.049	<b>4.37</b>
<b>M2 oocytes*</b>	8.7±0.6, 55	10.3±0.4, 186		0.050	<b>4.26</b>
<b>Long stim. / short stim.*</b>	29/26	129/57	81%/68%	0.02	<b>3.75</b>
<b>Days of stim.</b>	10.62±0.3, 55	10.67±0.2, 186		0.87	-
<b>E2 levels</b>	11090±735, 55	11960±443, 186		0.338	-
<b>P4 levels</b>	1.256±0.09, 55	1.24±0.08, 186		0.938	-
<b>Thickness of endo.</b>	10.96±0.3, 55	10.64±0.19, 186		0.41	-
<b># of follicles</b>	14.4±0.79, 55	15.84±0.51, 186		0.166	-
<b># of ET embryos</b>	2.36±0.1, 55	2.20±0.004, 186		0.068	-
<b>D3 ET/D5 ET</b>	18/37	39/147	68%/79%	0.07	-
<b>ICSI / IVF</b>	17/38	63/123	78%/76%	0.65	-
<b>Fresh cycles/FET cycles</b>	<b>55/32</b>	<b>186/86</b>	<b>77%/73%</b>	<b>0.36</b>	-

Data with \* are statistically different (p<0.05)

### Conclusions

In a program with high pregnancy rate with IVF, it is useful to know that the cause of pregnancy failure after implantation appears to be associated with patient factors that are known to affect oocyte quality. The factors found to be associated with pregnancy loss after implantation in IVF are: age, number of mature oocytes retrieved, total dose of gonadotropins used, and day 3 FSH level.

**β-HCG levels most significantly predict the outcomes of viable pregnancy. A threshold of β-HCG level predicting a failure of viable pregnancy is 93 IU/ml according to the equation derived from the logistic regression.**