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Title

Technological Advancements Translate to Bigger Babies: An 11 Year Trend in ART Outcome at a Single Practice

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Objective:
In vitro fertilization and embryo transfer (ET) has been used successfully for almost 30 years and accounts for 1-4% of annual conceptions. There has been a longstanding association of adverse perinatal outcomes, such as low birthweight and prematurity, associated with IVF use; a trend that has been attributed to the high proportion of multiple gestations associated with multiple embryos being transferred. Improvements in laboratory technology and clinical practice have allowed IVF to evolve into a safer, more effective and efficient treatment. This study examined changes in clinical and laboratory practice and their influence on neonatal birthweights over the past eleven years at a single, private IVF center.

Design:
Retrospective cohort analysis

Materials and Methods:
Electronic medical records database of neonates born from women who underwent autologous IVF between January 2004 and July 2015, with ≥1 live born child were included. Patient and cycle demographics as well as trends in birth weights were analyzed. Student's t-test was used for continuous variables, and the X^2 test was used for categorical variables. Significance was confirmed at $p<0.05$.

Results:
A total of 5782 cycles with birthweight reported were included. All patient demographics, cycle characteristics and clinical outcomes are shown in Table 1. Single ET cycles increased from 9.5% in 2004 to 60.0% in 2015. The average birth weight increased from 2869.1±797.3 grams to 3126.8±723.3 grams, a difference of +257.7 grams ($p<0.05$). The average days of gestation increased from 263.8±23.2 to 269.6±23.9, a positive difference of +6.2 days ($p<0.05$). The

proportion of neonates with Low Birthweight (<2500 grams) decreased from 28.0% to 15.7%. The proportion of neonates with Extremely Low Birthweight (<1000 grams) decreased from 3.1% to 1.9%. The proportion of patients with a preterm delivery (32-37 weeks) decreased from 23.2% to 13.1%.

Conclusions:

Current techniques including extended embryo culture, genomic embryo selection, and transfer of a single thawed euploid embryo into synthetically prepared endometrium have the potential to improve the social, medical, financial, and psychological aspects of IVF. Our longitudinal analysis of data study suggests that the reduction in number of embryos transferred is a major driver of the 8% overall increase in neonatal birthweight, 44% decrease in low birthweight, and 39% decrease in very low birthweight babies. Scientific advances have provided today's clinicians with the tools to precisely select embryos, reduce multiple pregnancy and birth, and redefine success as the chance of a singleton term birth.

Support:

None.

Table:

	2004	2010	2015	Difference 2004 to 2015	Stats
Cycles	n=818	1465	n=892		
Age	36.3±4.7	36.5±4.6	36.1±4.6	-0.2	NS
BMI	24.4±4.5	24.1±4.7	24.0±4.5	-0.4	NS
Antagonist Protocol	27.9% (202/724)	45.9% (672/1465)	81.6% (373/457)		p<0.05
Down Regulation Protocol	55.5% (402/724)	31.2% (457/1465)	1.5% (7/457)		p<0.05
GND usage (IU)	3469.4±1166.6	3512.3±1480.0	3803.2±1367.2	+333.8 IU	p<0.05
Oocytes retrieved	14.4±7.9	13.9±8.2	14.0±8.9	-0.4 oocytes	NS
Day 5/6 ETs	45.6% (373/818)	34.2% (501/1465)	98.5% (879/892)		p<0.05
Embryos transferred	2.7±1.1	2.6±1.2	1.5±0.6	-1.2 embryos	p<0.05
Cycles with a SET	9.5% (78/818)	14.7% (215/1465)	60.0% (535/892)		p<0.05
Cycles with ≥4 embryos transferred (age range 21-27)	21.6% (177/818)	2.1% (300/1465)	0.4% (4/892)		p<0.05
OHSS (moderate or severe)	8.1% (59/724)	6.0% (80/1332)	0.9% (4/457)		p<0.05
Birthweight (all cycles)	2869.1±797.3	2899.4±723.4	3126.8±723.3	+257.7 grams	p<0.05
Birthweight (1 live birth)	3237.4±647	3201.4±563.5	3282.0±658.9	+44.6 grams	NS
Birthweight (≥2 live births)	2210.6±590.7	2269.0±606.6	2357.6±506.4	+147 grams	NS
Low Birthweight (<2500 grams)	28.0% (229/818)	27.0% (395/1465)	15.7% (140/892)		p<0.05
Extremely Low BW (<1000 grams)	3.1% (25/818)	2.5% (36/1465)	1.9% (17/892)		p<0.05
Days of gestation (all cycles)	263.8±23.2	264.6±24.0	269.6±23.9	+6.2 days	p<0.05

Days of gestation (1 live birth)	271.8±19.1	271.1±23.0	273.6±21.8	+1.8 days	NS
Days of gestation (≥2 live births)	248.7±22.8	250.9±18.2	253.0±16.2	+4.5 days	NS
Preterm (32-37 weeks)	23.2% (190/818)	24.1% (353/1465)	13.1% (117/892)		p<0.05
Very Preterm (<32 weeks)	5.1% (42/818)	4.7% (69/1465)	4.5% (40/892)		p<0.05

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Down Regulation Protocol	55.5% (402/724)	31.2% (457/1465)	1.5% (7/457)		p<0.05
Day 5/6 ETs	45.6% (373/818)	34.2% (501/1465)	98.5% (879/892)		p<0.05
Embryos transferred	2.7±1.1	2.6±1.2	1.5±0.6	-1.2 embryos	p<0.05
Cycles with a SET	9.5% (78/818)	14.7% (215/1465)	60.0% (535/892)		p<0.05
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