



AMERICAN SOCIETY FOR
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Title

Fertility Outcomes in Women With Hypopituitarism Who Undergo ART Treatment

Authors:

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Objective:

Patients with hypopituitarism (HP) face many reproductive challenges. A small number of studies evaluating these patients report sub-optimal outcomes both in terms of pregnancy rates and pregnancy outcome. While new-age fertility advancements have been thought to improve treatment outcome for these patients, present data remains limited. This study shares its experience treating HP patients over the course of 13 years.

Design:

Retrospective

Materials and Methods:

Patients identified with HP and who underwent a fresh IVF cycle between July 2002 and July 2015 were included. Patients had a prior pan- or partial hypopituitarism diagnosis and required pituitary hormone replacement therapy. For this study, hypopituitarism was defined a deficiency in at least one anterior pituitary hormone in addition to gonadotropins. Patients with tubal factor or severe male factor infertility using donor sperm, age-matched (<38 years), and treated within the study period were identified as study controls. Student's t-test was used for continuous variables, X² test for categorical variables, and significance was confirmed a p<0.05.

Results:

Patients with HP (n=67) underwent 91 fresh IVF cycles and were compared to 871 controls that underwent 1235 IVF cycles (Table 1). Patients with HP were thinner (BMI: 21.7±4.5 vs. 25.0±5.9, p<0.05), had higher AMH level (3.9±4.8 vs. 2.6±2.1, p<0.05), lower Day 3 FSH (2.3±3.0 vs. 6.1±3.3), LH (1.3±2.2 vs. 3.9±2.5) and estradiol (E₂) (29.8±12.2 vs. 41.7±26.2) than controls. Patients with HP required increased total gonadotropin dose (4201.7±1888.5 IU vs. 3674.7±1758.5 IU, p<0.05) yet had similar levels of hormones levels at surge and post-trigger as compared to controls. HP patients had a similar number of embryos ongoing at the pronuclear and blastocyst stage compared to controls. HP patients had decreased number of embryos transferred (1.5±1.2 vs. 2.2±0.9). All clinical outcomes analyzed were similar between study cohorts: pregnancy rate (PR) 61.5% (56/91) vs. 60.2% (744/1235); clinical PR 52.7% (48/91) vs. 51% (631/1235); early pregnancy loss rate 18.7% (17/91) vs. 15.5% (192/1235) and live birth rate 46.3% (38/82) vs. 44.1% (545/121235). Lastly, neonates born to HP patients were shown to have similar birthweight and gestational age.



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Conclusions:

Even though pituitary hormone deficiency beyond gonadotropins has been correlated with major adverse effect on outcome, patients with HP can be reassured that modern IVF treatment has the potential to help them realize their goal of achieving successful pregnancy. In this study, patients with HP had similar clinical pregnancy, early pregnancy loss and live birth rates when compared to controls. To date, this study provides the largest analysis of HP patients undergoing IVF. This study provides clinicians with justification to recommend IVF treatment to patients with HP, while reassuring patients that the ability to pivot away from prior adverse perception, instills greater confidence within patients seeking treatment, and serves to remind us of the magnitude ART has on building families.

Support:

None.

Table:

	Hypopituitarism	Controls	
	n=91	n=1235	
Cycles			
Age	33.9±4.6 (95% CI 32.9 – 34.8)	33.9±3.1 (95% CI 33.7-34.0)	NS
BMI	21.7±4.5 (95% CI 20.5 – 22.8)	25.0±5.9 (95% CI 24.5-25.5)	p<0.05
AMH	3.9±4.8 (95% CI 2.1 – 5.7)	2.6±2.1 (95% CI 2.3-3.0)	p<0.05
Day 3 E ₂	29.8±12.2 (95% CI 27.0 -32.6)	41.7±26.2 (95% CI 40.0-43.5)	p<0.05
Day 3 FSH	2.3±3.0 (95% CI 1.5 – 3.0)	6.1±3.3 (95% CI 5.8-6.3)	p<0.05
Day 3 P ₄	0.3±0.2 (95% CI 0.3 – 0.4)	0.4±0.3 (95% CI 0.4-0.5)	NS
Day 3 LH	1.3±2.2 (95% CI 0.7 – 1.8)	3.9±2.5 (95% CI 3.7-4.1)	p<0.05
Follicles >Eq14 at surge	12.3±6.0 (95% CI 11.0 – 13.6)	11.9±5.8 (95% CI 11.5-12.2)	NS
Endometrium at surge	9.3±1.7 (95% CI 9.0 – 9.7)	10.2±1.9 (95% CI 10.1-10.3)	NS
E2 at surge	2173.9±965.2 (95% CI 1972.9 – 2374.9)	2260.4±1050.4 (95% CI 2201.6-2319.2)	NS
P4 at surge	0.7±0.4 (95% CI 0.6 – 0.8)	1.0±0.6 (95% CI 1.0-1.0)	NS
GND Cumulative Dose	4201.7±1888.5 (95% CI 3808.4 – 4595.0)	3067.5±1284.6 (95% CI 2995.8-3139.3)	p<0.05
Stim duration	10.5± 1.9 (95% CI 10.1 – 10.9)	8.6±1.2(95% CI 8.5 – 8.7)	
Day +1 E ₂	2831.9±1376.9 (95% CI 2545.2 – 3118.7)	2930.4±1432.4 (95% CI 2849.9-3011.0)	NS
Day +1 P ₄	3.1±1.9 (95% CI 2.7 – 3.5)	3.7±2.0 (95% CI 3.5-3.8)	NS
Day +1 LH	83.2±66.6 (95% CI 21.6 – 144.8)	75.2±43.1 (95% CI 66.2-84.2)	NS
Day +1 β-hCG	182.6±136.4 (95% CI 153.2 – 212.1)	150.0±98.0 (95% CI 144.0-156.1)	p<0.05
Oocytes Retrieved	14.4±8.9 (95% CI 12.5 – 16.2)	14.9±8.0 (95% CI 14.5-15.4)	NS
Day 1 Ongoing	8.8±6.0 (95% CI 7.5 – 10.1)	8.7±5.8 (95% CI 8.4-9.0)	NS
Day 5 Ongoing	4.3±4.8 (95% CI 3.2 – 5.3)	3.9±4.4 (95% CI 3.6-4.1)	NS
ET count	1.5±1.1 (95% CI 1.3 – 1.7)	2.2±0.9 (95% CI 2.1-2.2)	p<0.05
Day +16 E ₂	690.7±905.4 (95% CI 433.4 – 948.1)	428.6±578.3 (95% CI 392.6-464.6)	NS
Day +16 P ₄	42.1±54.1 (95% CI 26.7 – 57.5)	35.0±37.7 (95% CI 32.7-37.4)	NS
Gestational age (weeks)	37.3±3.7 (95% CI 36.1 – 38.5)	37.5±5.0 (95% CI 37.0-37.9)	NS
Preterm (<37 weeks)	29.3% (24/82)	31.1% (380/1235)	NS



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Birthweight	2571.7±670.1 (95% CI 2341.5 – 2801.9)	2842.2±831.5 (95% CI 2768.3- 2916.2)	NS
Low Birthweight (<2500 gr)	39.5% (15/38)	29.5% (364/1235)	NS
Pregnancy Rate	61.5% (56/91)	60.2% (744/1235)	NS
Clinical Pregnancy Rate	52.7% (48/91)	51% (631/1235)	NS
Early Pregnancy Loss Rate	18.7% (17/91)	15.5% (192/1235)	NS
Live Birth Rate	46.3% (38/82)	44.1% (545/121235)	NS

	Hypopituitarism (n=91)	Controls (n=1235)			Hypopituitarism (n=91)	Controls (n=1235)	
Age	33.9±4.6 (95% CI 32.9 – 34.8)	33.9±3.1 (95% CI 33.7- 34.0)	NS	Oocytes Retrieved	14.4±8.9 (95% CI 12.5 – 16.2)	14.9±8.0 (95% CI 14.5-15.4)	NS
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Endometrium at surge	9.3±1.7 (95% CI 9.0 – 9.7)	10.2±1.9 (95% CI 10.1- 10.3)	NS	Day +16 P ₄	42.1±54.1 (95% CI 26.7 – 57.5)	35.0±37.7 (95% CI 32.7-37.4)	NS
E2 at surge	2173.9±965.2 (95% CI 1972.9 – 2374.9)	2260.4±1050.4 (95% CI 2201.6-2319.2)	NS	Gestational age (weeks)	37.3±3.7 (95% CI 36.1 – 38.5)	37.5±5.0 (95% CI 37.0-37.9)	NS
P4 at surge	0.7±0.4 (95% CI 0.6 – 0.8)	1.0±0.6 (95% CI 1.0-1.0)	NS	Preterm (<37 weeks)	29.3% (24/82)	31.1% (380/1235)	NS
GND Cumulative Dose	4201.7±1888.5 (95% CI 3808.4 – 4595.0)	3067.5±1284.6 (95% CI 2995.8-3139.3)	p<0.05	Birthweight	2571.7±670.1 (95% CI 2341.5 – 2801.9)	2842.2±831.5 (95% CI 2768.3-2916.2)	NS
Stim duration	10.5± 1.9 (95% CI 10.1 – 10.9)	8.6±1.2(95% CI 8.5 – 8.7)		Low Birthweight (<2500 gr)	39.5% (15/38)	29.5% (364/1235)	NS
Day +1 E ₂	2831.9±1376.9 (95% CI 2545.2 – 3118.7)	2930.4±1432.4 (95% CI 2849.9-3011.0)	NS	Low Birthweight (<2500 gr)	39.5% (15/38)	29.5% (364/1235)	NS
Day +1 P ₄	3.1±1.9 (95% CI 2.7 – 3.5)	3.7±2.0 (95% CI 3.5-3.8)	NS	Pregnancy Rate	61.5% (56/91)	60.2% (744/1235)	NS
Day +1 LH	83.2±66.6 (95% CI 21.6 – 144.8)	75.2±43.1 (95% CI 66.2- 84.2)	NS	Clinical Pregnancy Rate	52.7% (48/91)	51% (631/1235)	NS
Day +1 β-hCG	182.6±136.4 (95% CI 153.2 – 212.1)	150.0±98.0 (95% CI 144.0-156.1)	p<0.05	Live Birth Rate	46.3% (38/82)	44.1% (545/121235)	NS