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## Pregnancy Outcome with In Vitro Fertilization-Embryo Transfer According to Age in Women with Diminished Oocyte Reserve (DOR) using a Follicle Stimulating Hormone Receptor Up-Regulation Technique

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# Pregnancy outcome with in vitro fertilization-embryo transfer according to age in women with diminished oocyte reserve (DOR) using a follicle stimulating hormone receptor upregulation technique

Brooke Neumann, Jerome H. Check, Carrie Wilson, Michael Sobel, Jung K. Choe

OBJECTIVE: RESULTS: CONCLUSIONS:

About 18 years ago, one of the top IVF centers published a study and found that women with DOR did not have any live deliveries at any age in women with a day 3 serum FSH exceeding 18 mIU/mL. The failure to achieve a live delivery may have been related to the ovarian hyperstimulation regimen with possible down regulation of the FSH receptor needed to produce a key enzyme needed for successful implantation. The purpose of this 25-year retrospective review was to evaluate the efficacy of a specific type of mild stimulation referred to as the FSH receptor up-take technique on achieving live deliveries in women with extremely low egg reserve, and to determine the confounding effect of age.

There were 1285 transfers of single day 3 embryos performed. A clinical and live delivered pregnancy rate was seen in 71 and 62 of 262 transfers (27% and 23.7%, respectively) in women < age 35. A clinical and live delivered pregnancy was seen in 79 and 57 of 471 transfers (16.8% and 12.1%, respectively) in women aged 36-39. For women 40-42, clinical and live delivered pregnancies occurred in 71 and 34 of 552 transfers (12.9% and 6.2%, respectively). Overt ovarian failure (as defined by >1 year of amenorrhea, no menses with progesterone treatment and withdrawal, serum E2 <20 pg/mL and serum FSH >60 mIU/mL) was found in 334 of the 1285 transfers (26.0%).

Using this FSH receptor up-regulation technique, live delivered pregnancy rates in women with severe DOR seem to be about twice as high in women age <35 vs. 36-39 and 4 times higher than women 40-42. Women 36-39 are twice as likely to have a baby as women aged 40-43 when there is severe DOR.

#### **MATERIALS & METHODS:**

Inclusion criteria were as follows: 1) all ages up to 42.9 years, 2) the use of the FSH receptor upregulation stimulation technique, 3) only 1 embryo was created which had >4 blastomeres on day 3, 4) based on day 3 serum FSH (>12 mIU/mL) and/or serum anti-mullerian hormone (AMH) levels (<1ng/mL), there was evidence of DOR. Both clinical (ultrasound documented pregnancy at 8 weeks) and live delivered pregnancy rates were determined, 5) all cycles over a 25-year time were included. The same patient could be used more than once. The main tenets of the FSH receptor upregulation technique are not only to use minimal FSH stimulation (usually no more than 75-150 IU FSH per day), but not to use any FSH if the serum level was >12 mIU/mL. This allows the endogenous FSH to drive the follicular maturation, but when dropping levels of serum FSH is occurring related to rising serum estradiol (E2), one may add a mild dosage of FSH to either boost the 1 dominant follicle to full maturation, or to try to recruit more than one follicle. Ethinyl estradiol, 20 mcg, would be used for a short follicular phase or to restore down-regulated FSH receptors in women who appeared to be in overt menopause.

#### **IMPACT STATEMENT:**

These data will hopefully influence other fertility centers to encourage their own success rates in a similar population of patients and if their success rates are inferior perhaps persuade them to a evaluate the FSH receptor up-regulation technique to determine if this stimulation protocol improves pregnancy outcome.

