Multivariate analysis of the association between oocyte donor characteristics, including basal follicle stimulating hormone (FSH) and age, and IVF cycle outcomes

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Objective: To determine whether oocyte donor FSH and age are independently associated IVF cycle success.
Design: Retrospective cohort study.
Setting: University hospital-based IVF clinic.
Patient(s): Three hundred twelve donor/recipient pairs undergoing oocyte donation IVF.
Main Outcome Measure(s): Number of mature oocytes and embryos, clinical pregnancy, and live birth rates.
Result(s): Donors' basal FSH levels were not associated with IVF cycle outcomes. However, for every year increase in donor age, the number of mature oocytes decreased by 0.39 and the number of embryos decreased by 0.25 resulting in 1 less embryo for each 4-year increase in age, even in young donors. For every 100 pg/mL increase in estradiol on the day of hCG administration, the number of mature oocytes increased by 0.49 and the number of embryos increased by 0.36. For each additional 75 IU of gonadotropin used during stimulation, the likelihood of pregnancy and live birth decreased by 3.5%.
Conclusion(s): Donor oocyte IVF cycle outcomes were not associated with donor basal FSH. However, donor age and estradiol level on the day of hCG administration were significantly associated with numbers of mature oocytes and embryos obtained, and the amount of gonadotropin used in the stimulation was significantly associated with the likelihood of pregnancy and live birth. (Fertil Steril® 2010;94:1292–5. ©2010 by American Society for Reproductive Medicine.)

Key Words: Oocyte donation, egg donation, donor FSH, donor age

Oocyte donation is increasingly used to help couples have families. The number of donor oocyte IVF cycles in 2007 in the United States alone increased to over 14,000, representing 11% of total IVF cycles (1). Oocyte donation involves coordination and treatment of two individual patients is more costly than traditional IVF, and donor availability is limited, making optimization of outcomes paramount in these cycles.

Few studies have examined donor characteristics that are predictive of success in these cycles. Publications to date have focused on the relationship between donor age and prior fertility and IVF outcomes. Results have been conflicting, and the number of donors has been small with most containing <300 IVF cycles (2–4). Previous studies included individuals that donated multiple times, having the potential to overrepresent donors with favorable outcomes, and have also not consistently controlled for recipient characteristics (3–6).

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In the present study, which includes a large population of individual donors, we examined the relation between donor characteristics, including basal FSH and age, and IVF cycle outcomes. Furthermore, we attempted to identify a threshold of donor FSH and age that suggested a distinct decrease in the likelihood of successful cycle outcome.

MATERIALS AND METHODS

All oocyte donation IVF cycles that started from January 1, 2000 to December 31, 2006 at a large university hospital-based IVF clinic were identified after hospital institutional review board approval was obtained. The investigators have no conflict of interest to report. Only the first oocyte donation per individual in the study years was included to avoid enriching the population with donors who were more likely to be successful by being used in repetitive cycles. Three hundred twelve donor/recipient pairs met the eligibility criteria. In our oocyte donation program, only known donors were accepted after age 34, and most anonymous donors were in their twenties. Donors with an FSH ≥10 were encouraged not to donate. Recipients were down-regulated on leuprolide acetate and then placed on estradiol to maintain serum levels >180 pg/mL, with intramuscular or vaginal progesterone beginning the night of oocyte retrieval. Oocyte donors were started on leuprolide acetate 0.5 mg dropping to 0.25 mg after down-regulation was achieved. Donor age and FSH were the criteria used to select gonadotropin dose given no prior cycle information was available, with older donors and donors with FSH ≥8 more often receiving higher doses. Most of our donors were stimulated with FSH alone, with only 8% receiving both FSH and hMG. Stimulation was generally started at 150–225 IU per day for donors <30 years of age and 187–225

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IU per day in donors up to age 35 (range = 75–525 IU per day). Donors aged 35 received higher doses of gonadotropins, and those in their early 40s were on antagonist or microdose protocols.

All IVF outcome variables were defined from data abstracted from the medical record. Outcomes per donor stimulation included the number of mature oocytes retrieved, fertilization rate, and number of embryos obtained. IVF outcomes per cycle using only the first embryo transfer per stimulation included clinical pregnancy, live birth, and implantation rate (number of gestational sacs/number of embryos transferred). Clinical pregnancy was defined as ultrasound visualization of a gestational sac excluding ectopic and chemical pregnancies; live birth was defined by the birth of at least one live-born child. Oocyte donor and recipient characteristics were abstracted from the medical record. Donor variables included basal FSH (drawn on cycle day 2, 3, or 4), age at the start of ovarian stimulation (months), prior gravidity, starting dose of gonadotropin used for stimulation, total amount of gonadotropin used for stimulation, days of stimulation before hCG administration, estradiol level (pg/mL) on the day of hCG administration, and known versus anonymous donation. Recipient variables included age at the start of the IVF cycle (months), prior gravidity, history of prior uterine surgery (including previous dilation and curettage, myomectomy, operative hysteroscopy, or cesarean section), and number of embryos transferred. Many of the above variables were chosen because previous reports have suggested potential relations to IVF outcomes, including donor FSH, age, and prior gravidity. Basal estradiol levels have not been found to predict IVF outcomes so were not included in the analysis (7). Other variables had the potential for confounding such as previous uterine surgery possibly causing intrauterine adhesions, thereby impacting pregnancy and live birth rates, the number of embryos transferred impacting pregnancy rates, and the starting dose of gonadotropin being chosen based on donor age and FSH. The total amount of gonadotropin used in stimulation, days of stimulation to hCG administration, and estradiol level on the day of hCG administration indicate the response of the oocyte donor and were chosen given the potential prognostic significance for IVF outcomes.

To search for a threshold of donor FSH and age above which donation was less likely to be successful, clinical pregnancy and live birth rates were compared after grouping donors based on basal FSH and age. Groups were based on percentile of FSH or age within the cohort. FSH group 5 was used as the referent group when comparing IVF outcomes between FSH groups. Age group 4 was used as the referent group when comparing IVF outcomes between age groups (Table 1).

The distribution of donor, recipient, and cycle characteristics were calculated. Preliminary exploratory data analysis was used to evaluate variable distributions and to assess relations among key covariables. Multivariate logistic regression analyses were performed to assess the association between individual donor and recipient characteristics and clinical pregnancy and live birth rates, and also to compare these outcomes between FSH and donor groups. Multivariate linear regression analyses were performed to assess the association between individual donor and recipient characteristics and the number of mature oocytes retrieved, number of total embryos obtained, fertilization rates, and implantation rates. In the multivariate analysis, when any one variable was missing, that pair was excluded, resulting in 218 total pairs. The most frequent missing variable was donor basal FSH, followed by donor gravidity, because not all donors laboratory screening or history was performed at our institution and complete medical records were not always available for review. Preliminary data analysis showed a history of uterine surgery and known versus anonymous donation did not significantly affect outcomes, and were excluded from the multivariate analysis. SAS statistics software was used to calculate statistical analysis; all given Wald *P* values are two sided.

RESULTS

Donor basal FSH ranged from 1.4 to 12.8 mIU/L and donor age ranged from 20.4 to 43.5 years (Table 2). Our cohort had an overall pregnancy rate of 52.9% and a live birth rate of 45.48% (Table 2). Pregnancy rates were also calculated by donor age range: donors <30 years (n = 200), pregnancy rate = 55%, donors 30–34.99 years (n = 71), pregnancy rate = 51%, donors 35–39.99 years (n = 34), pregnancy rate = 47%, donors 40 years and older (n = 4) pregnancy rate = 50%. No statistical difference existed between groups.

TABLE 1

Donor groups for nonlinear analyses when testing for FSH and age thresholds.

Donor group	Percentile represented by group	Range
FSH group		
1	0–10	≤3.90
2	11–25	3.91–5.00
3	26–50	5.01–6.30
4	51–75	6.31–7.65
5[a]	90	≥7.65
Age group		
1	0–5	≤21.80
2	6–10	21.81–22.20
3	11–25	22.21–23.80
4[a]	26–50	23.81–27.25
5	51–75	27.26–32.20
6	76–90	32.21–36.0
7	91–95	36.01–37.80
8	96–100	≥37.80

Note: Range is either represented as basal FSH (mIU/mL) or years.
[a] Referent group when comparing outcomes between groups.

Barton. Oocyte donor age, FSH, and IVF outcomes. Fertil Steril 2010.

Multivariate analysis revealed donor basal FSH did not significantly affect clinical pregnancy or live birth rates (*P* value, test for linear trend = 0.58 and 0.85, respectively) (Table 3). Similarly, number of mature oocytes, total number of embryos, fertilization rate, and implantation rate were not significantly associated by donor basal FSH level. However, donor age, estradiol level on the day of hCG administration, and the amount of gonadotropin used for ovarian stimulation did significantly affect various IVF cycle outcomes.

Donor age was inversely related to the number of mature oocytes and embryos obtained per cycle. For every year increase in donor age, the number of mature oocytes decreased by 0.39 (*P* value, test for linear trend <.01) and the number of embryos decreased by 0.25 (*P* value, test for linear trend = .01) (Table 3). This translated to one less embryo for every 4-year increase in donor age, even for donors in their twenties.

Estradiol level on the day of hCG administration was directly related to the number of mature oocytes, total number of embryos, and number of embryos frozen per cycle. For every 100 pg/mL increase in estradiol level on the day of hCG administration, the number of mature oocytes increased by 0.49 (*P* value, test for linear trend <.01) and the total number of embryos increased by 0.36 (*P* value, test for linear trend <.01) (Table 3). Therefore, an estradiol level difference of 300 pg/mL was associated with a difference of just over one embryo.

The amount of gonadotropin used for oocyte donor ovarian stimulation was inversely related to clinical pregnancy and live birth rates. For each additional 75 IU of gonadotropin used during stimulation, the likelihood of pregnancy decreased by 3.45% (*P* value, test for linear trend = .02) (Table 3). Therefore, an additional 225 IU of gonadotropin was associated with a 10.35% lower likelihood of pregnancy per cycle. The amount of gonadotropin used was also significantly associated with the likelihood of live birth rate with