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Assisted Reproduction

Factors Associated with an Optimal Pregnancy Outcome in an Oocyte Donation Program

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***Purpose*:** To identify donor and recipient variables that may have a significant impact on pregnancy outcome in order to optimize results of an oocyte donation program.
***Method*:** Retrospective analysis through a Generalized Estimating Equation (GEE) approach to clustered and binary clustered data, linear mixed effects model, scatter plot smoothing functions, and receiving operator characteristics (ROC) curves. *Setting*: University-based center. *Intervention(s):* None. *Main outcome measures*: Pregnancy and implantation rates. *Patients*: 257 donation and transfer cycles.
***Result(s)*:** Overall results were as follows: clinical pregnancy rate, 47%; implantation rate, 22%; abortion rate, 19%; and overall multiple pregnancy rate, 35%. The total reproductive potential was 60%. Implantation and pregnancy rates were not significantly related to any variable from donors or recipients. Abortion rate increased significantly with donors' increased basal serum LH. Pregnancy rate was significantly enhanced with improved embryo quality. In donors stimulated more than once, the pregnancy rate was 84%.
***Conclusion(s)*:** Although no single or combined donor or recipient variable(s) could be identified as predictor(s) of pregnancy, the data suggest that donors ≤33 years of age with basal cycle day 3 serum levels of FSH 4–8 IU/L, LH < 8 IU/L, and E2 < 70 pg/mL had an optimal outcome. Transfer of two selected embryos on day 3 yields a favorable pregnancy outcome while significantly decreasing the occurrence of multiple pregnancies. These policies, in addition to embryo cryopreservation, were associated with optimal pregnancy outcome in oocyte donation.

KEY WORDS: FSH; implantation; IVF; LH; Oocyte donation; pregnancy.

INTRODUCTION

According to the last report from the Centers for Disease Control and Prevention (CDC) (1), oocyte donation was performed in approximately 10% of all ART cycles carried out during that year in the United States. The reported live birth rate per transfer for oocyte donation was 41% using fresh embryos and 23% for cycles using cryopreserved-thawed embryos. On a theoretical basis, the success of oocyte donation may be influenced by various factors including age of the oocyte donor, quality, and number of embryos transferred, and age and endometrial receptivity of the recipient.

The age of the donor is one of the most important factors influencing outcome (2). Following the recognition of the "oocyte factor" the practice has developed toward the recruitment of healthy donors under 35 years of age showing a normal ovarian reserve (3). According to the same CDC report (1), the average number of embryos transferred per cycle of oocyte

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donation was 3.0. Although the American Society for Reproductive Medicine (ASRM) Practice Committee has published recently an oocyte donation guidelines (3–5), there is no general consensus regarding the number of embryos to transfer in this population in order to maximize pregnancy outcome while at the same time, diminishing the incidence of multiple pregnancies. Similarly, there is no general agreement on which is the best ovarian stimulation protocol to use in donors aiming to recover a cohort of fertilizable oocytes of highest developmental potential while minimizing the risk of ovarian hyperstimulation.

There are controversies regarding the impact of the age of the recipient on implantation and pregnancy outcome. While some investigators have found a lower pregnancy rate in recipients of more advance age (6), others have not observed this relationship (7). The preparation of the recipient's endometrium for embryo transfer is typically performed in estradiol (E_2)-progesterone-supplemented cycles. Endometrial preparation, endometrial sonographic appearance, and serum steroid hormonal levels have been signaled as important factors of success (8).

In this study, we investigated the impact of a variety of donor and recipient variables on the overall success of our oocyte donation program. The objective was to identify statistically valid factors to establish policies aimed to optimize pregnancy potential and to reduce the incidence of multiple births in this population.

MATERIALS AND METHODS

We analyzed all consecutive oocyte donation cycles performed between July 1999 and December 2001 at the Jones Institute for Reproductive Medicine. Donors and recipients signed appropriate consent forms to participate in the program. The Institutional Review Board at Eastern Virginia Medical School approved the study.

Donors

A total of 146 different donors were stimulated and they underwent 257 stimulation cycles. The oocyte donors' age ranged from 20 to 33 (mean 27 ± 3). They were presumed to be fertile on the basis of menstrual and/or pregnancy histories, had a normal pelvic and ovarian anatomy by ultrasound assessment, and had a normal ovarian reserve. Ovarian reserve was assessed by determination of basal cycle day 3 serum FSH, LH, and E_2 levels (9). Serum hormone levels were measured with a microparticle enzyme immunoassay (MEIA-IMX: Abbott Laboratories, Abbott Park, IL). The intraassay coefficients of variation were 4.3, 4.1, and 6.1% for FSH, LH, and E_2, respectively. The interassay coefficients of variation were 4.9, 5.8, and 8.2% for FSH, LH, and E_2, respectively. The lower limits of sensitivity were as follows: LH = 1.0 mIU/mL, FSH = 1.0 mIU/mL, and E_2 = 25 pg/mL, respectively. The regression equations to convert RIA to IMX are as follows: IMX FSH = 0.46 × RIA − 2.2; IMX LH = 0.3 × RIA − 1.1; IMX E_2 = 1.26 × RIA − 1.5. All donors underwent serum testing for Human Immunodeficiency Virus, Cytomegalovirus, Syphilis, and Hepatitis B and C, and were subjected to a psychological evaluation, following ASRM guidelines (3,5).

Donors underwent controlled ovarian hyperstimulation as previously described (10). Briefly, a long protocol for pituitary desensitization was carried out, with daily administration of 0.5 mg sc of leuprolide acetate (Lupron, Tap Pharmaceuticals, Abbott Park, IL) starting in the mid-luteal phase of the previous cycle. After the menstrual period, the dose of leuprolide was decreased to 0.25 mg sc daily until human Chorionic Gonadotropin (hCG) administration. Gonadotropin stimulation using a recombinant FSH (Gonal F; Serono Laboratories, Randolph, MA) was initiated on day 3 after menses at the dose of 225 IU/L, and then continued in a step-down fashion. Recombinant FSH was continued until the lead follicles were ≥16 mm in largest diameter. Ultrasound-guided transvaginal oocyte retrieval was performed 35 h after hCG. The maturational status of the oocytes was recorded according to the criteria of Veeck *et al.* (11). Mature oocytes were classified as metaphase II at the time of aspiration. Sperm processing and fertilization procedures (standard insemination or ICSI used in the presence of a male factor) were performed as previously described (12).

Recipients

A total of 231 recipient couples served by the 146 donors were studied. All women demonstrated normalcy of the uterine cavity by histerosalpingography, hydrosonography, or hysteroscopy. The recipients' age ranged from 25 to 54 years (mean 41 ± 5); they had been offered oocyte donation because of advanced reproductive age, previous poor ovarian response, repeated failure of in vitro fertilization (IVF) cycles, premature ovarian failure, or risk of genetic disease.

Endometrial preparation of the recipients was performed with transdermal E_2 (Vivelle, Ciba-Geigy Corporation, Summit, NJ) with a dose of 0.2 mg on days 1, 3, and 5, 0.3 mg on days 7 and 9, and 0.4 mg on days 11 and 13. Thereafter, the dose was decreased to 0.2 mg/day every other day .The administration of intravaginal progesterone Prometrium (Prometrium; Solvay Laboratories, Marietta, GA) at the dose of 200 mg, three times a day, was begun on day 15. The initiation of the follicular phase was synchronized with the donor's cycle using either birth control pills or leuprolide acetate (13). Endometrial thickness and pattern were assessed on day 15 (prior to the initiation of P4 supplementation) by transvaginal ultrasonography following previously reported methods (14,15).

Embryo transfer was performed on day 3 (day 18 of the supplemented cycle). The number of embryos transferred ranged from 2 to 4 following ASRM guidelines (3–5). Typically, the three best embryos were transferred based upon highest morphology score (11) and more advanced cleavage status. Surplus embryos were cryopreserved at the pronuclear or cleavage stages following protocols published elsewhere (16,17) and transferred in E_2-progesterone-supplemented cycles. At 12 days after the embryo transfer, a blood test for ß-hCG assessment was performed and if positive was repeated 48–72 h later. Transvaginal ultrasonography was performed at 6–7 weeks gestation to assess the presence of a gestational sac and viability.

Statistical Analysis

Fertilization rate was defined as the number of oocytes showing diploid fertilization divided by the total number of mature oocytes inseminated. For the purpose of the present analysis, embryos were further classified according to a "Total Embryo Score" that consisted of the combination of morphology grading and the cleavage stage of the best two embryos transferred. Embryos classified as score 1 were grade 1 or 2 according to the criteria of Veeck (11) with $\geq$7 cells; score 2 embryos were grade 3 with $\geq$5 or more cells, or grade 1 or 2 with 5–7 cells; and score 3 embryos were grade 4 or 5 with <5 cells. A clinical pregnancy was defined as the presence of a gestational sac by ultrasound at 6–7 weeks gestation. The implantation rate was calculated as the number of gestational sacs seen by first trimester ultrasound divided by the total number of embryos transferred. The total reproductive potential (an expression of cycle efficiency resulting from the transfer of fresh and cryopreserved embryos from a single stimulation) was calculated as previously reported (18).

Data were incorporated into an Excel® file and independently analyzed by a biostatistician (see acknowledgment) using chi-square analysis, linear mixed effects model, scatter plot smoothing functions, receiving operator characteristics (ROC) curves, and Generalized Estimating Equation (GEE) as appropriate. GEE is a particularly powerful and versatile approach to the analysis of both continuous and categorical outcome variables that employs repeated measures regression analyses under the GEE method to analyze interaction effects. The GEE procedure provides robust estimates of population averaged effects and is especially advantageous when the objective is to make inferences about group differences (19,20). Statistical differences were determined at $P < 0.05$. Data are presented as mean ± standard deviation.

RESULTS

Overall Results

We analyzed 257 stimulation cycles resulting in 257 fresh transfer cycles and 96 cycles of transfer of cryopreserved-thawed embryos. Donor and recipient characteristics are shown in Table I. Intracytoplasmic sperm injection (ICSI) was performed in 28% of the cycles while standard IVF was carried out in the others. The overall fertilization rate was 80%, and it was not significantly different between ICSI and standard IVF (data not shown). Overall, a mean of 3 ± 1 embryos were transferred.

Table I. Characteristics of Donors abd Recipients

	Mean ± SD	Range
Donors		
Age (years)	27 ± 3	(20–33)
Day 3 FSH (IU/L)	6 ± 1	(2–9)
Day 3 LH (IU/L)	5 ± 2	(1–12)
Day 3 E2 (pg/mL)	47 ± 16	(25–100)
Suppressed day-3 E2 (pg/mL)	40 ± 22	(25–100)
Number of FSH ampoules used	25 ± 6	(9–50)
Peak E2 (pg/mL)	2600 ± 1300	(500–7000)
Day of hCG administration	12 ± 1	(10–16)
Number of mature oocytes retrieved	13 ± 5	(4–27)
Recipients		
Age (years)	41 ± 5	(25–54)
Day 15 endo. th. (mm)	9 ± 2	(3–20)
Day 15 E2 (pg/mL)	700 ± 500	(50–1600)
Day 15 P4 (ng/mL)	0.8 ± 0.2	(0.5–1.3)
Fertilization rate (%)	80	(33–100)
Number of embryos transferred	3 ± 1	(1–4)

The clinical pregnancy rate per transfer was 48% (123/257) in fresh cycles and 34% (32/96) in cryo-thaw cycles, while the implantation rate was 22 and 17% in fresh and cryo-thaw cycles, respectively. There were no significant differences in any of these rates when comparing IVF and ICSI (data not shown). In 65% (101/155) of such clinical pregnancies, one gestational sac was visualized by ultrasound at 6–7 weeks of gestation, in 25% of the pregnancies (40/155) two sacs were visualized, in 7% (11/155) three sacs, and in 3% (3/155) four gestational sacs were identified. The miscarriage rate was 19% (23/123) in fresh cycles and 12% (4/32) in cryo-thaw cycles. The total reproductive potential was 60%.

The live birth rate per transfer using fresh embryos was 39% (100/257) and for cryopreserved-thawed embryos was 29% (28/96). From a total of 128 resulting deliveries, 70% (90/128) were singletons, 28% (35/128) were twins, and 2% (3/128) were triplets. The observed difference between clinical pregnancies and delivered babies is mainly accounted for by the occurrence of miscarriage (either total or "vanishing" twin or triplet pregnancies) as only in 4% of all pregnancies selective reduction was performed as determined by patients' decision.

Analysis of Donor and Recipients Variables from Fresh Cycles

Donor Variables: Impact of Donors' Age and Ovarian Reserve on Ovarian Response. The impact of donors' age and ovarian reserve status on ovarian response was analyzed by the GEE approach. Ovarian response was assessed by the evaluation of the number of mature oocytes recovered, peak serum E_2 levels, total number of gonadotropin ampoules used, and day of hCG administration.

There was a significant ($P < 0.05$) and nonlinear relationship between basal cycle day 3 serum FSH levels and the number of mature oocytes retrieved (Fig 1). More oocytes were recovered in the range of serum day 3 FSH levels between 4 and 8 IU/L; fewer oocytes were obtained in donors with the lowest (<4 IU/L) and highest (>8 IU/L) FSH levels found. The maximum average of mature oocytes retrieved (13–14) was obtained when FSH values varied between 4.7 and 5.4 IU/L. On the other hand, the number of mature oocytes retrieved showed no association with donors' age, basal cycle day 3 LH, FSH:LH ratio or E_2 levels, or suppressed day 3 E_2 levels ($P > 0.4$ for all).

There was a significant and positive linear relationship between the total number of recombinant FSH ampoules used and basal cycle day 3 serum FSH levels ($P < 0.001$) (Fig. 2). The number of FSH ampoules used increased by two by every unit (IU/L) of day 3 FSH. The number of FSH ampoules used also showed a positive and significant relationship with the age of the donor. FSH ampoules increased at a rate of 0.56 ampoules for every year increase in donor age ($P < 0.01$) (data not shown). In addition, there was a significant and negative relationship between the total number of FSH ampoules used and the day 3 serum E_2levels following GnRH agonistsuppression. The number of ampoules decreased until an approximate E_2 value of 100 pg/mL and achieved a plateau thereafter ($P = 0.002$) (data not shown).

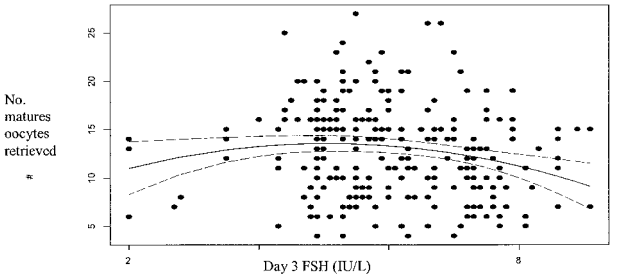

Fig. 1. Relationship between basal cycle serum day 3 and the number of matured oocyte recovered (GEE model regression and 95% confidence interval) ($P < 0.05$).

Donor Variables Related with Implantation, Pregnancy and Miscarriage. When analyzed by the GEE approach, neither the age of the donors nor the ovarian reserve or ovarian response variables were significantly related to pregnancy, implantation, or miscarriage rates ($P > 0.1$), with the exceptions of

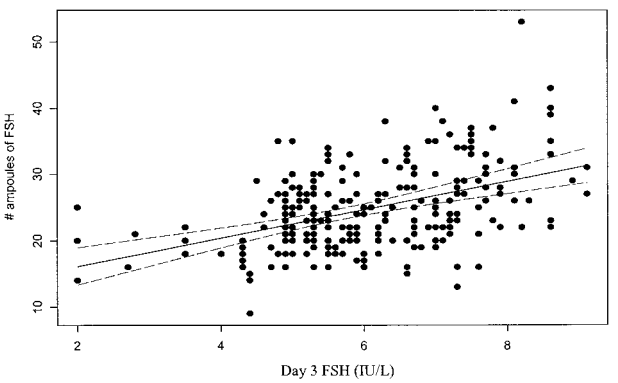

Fig. 2. Relationship between the total number of FSH ampoules used and basal cycle day 3 serum FSH levels. (GEE model regression and 95% confidence interval) ($P < 0.001$).

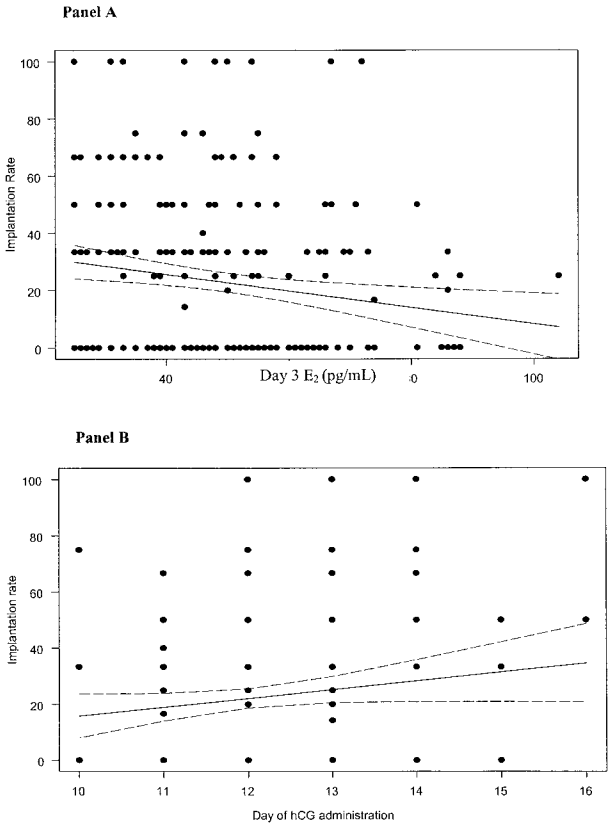

Fig. 3. Relationship between implantation rate and serum day 3 E2 levels (GEE regression model and 95% confidence interval) ($P = 0.004$) (Panel **A**) or day of hCG administration (GEE regression model and 95% confidence interval) ($P = 0.06$) (Panel **B**).

(a) decline in implantation rate with increasing basal cycle day 3 serum E_2 levels ($P = 0.004$, Fig. 3, panel A) and (b) a positive relationship of borderline significance between the day of hCG administration and implantation rate ($P = 0.06$, Fig. 3, panel B).

ROC curve analyses were performed to determine potential predictive cutoff values of dichotomous variables such as pregnancy and miscarriage. With implantation rate, a continuous variable, such analysis was performed using locally weighted variable-span scatterplot smoothing functions. Most of the donors variables analyzed (age, basal cycle day 3 serum FSH, E2, FSH:LH ratio, and number of mature oocytes recovered) were poor predictors of pregnancy or implantation rates (i.e., areas under the curve <0.58 and/or likelihood ratios <2).

On the other hand, basal cycle day 3 serum LH was a significantly associated with a higher occurrence of spontaneous miscarriage. A basal serum LH cutoff value of 9 IU/L resulted in a likelihood ratio of 4.3, meaning that the possibility of miscarriage increased four times over this limit (data not shown).

Although the number of mature oocytes recovered was not associated with the probability of conception, the implantation rate increased linearly up to 15–16 oocytes retrieved (not shown). In addition, although not statistically significant, the data indicated a clear trend for lower pregnancy rates when <6 mature oocytes were recovered ($P > 0.05$) (not shown).

Intra- and Interdonor Variabilities. Of the 146 donors studied, 66 underwent repeated stimulation cycles ranging from 2 to 7 (in a total of 187 stimulation cycles). In this group of donors, the clinical pregnancy rate was not significantly different when comparing results of consecutive cycles. Furthermore, there was no impact of additional stimulations on the donors' ovarian responses as examined by the number of mature oocytes recovered and requirement for gonadotropins in subsequent cycles (data not shown).

Of these 66 donors, 63 donated to more than one recipient. Eighty-four percent (53/63) of this selected group of donors produced at least one pregnancy, 48% of these donors establishing one pregnancy, and 36% establishing pregnancies in two or more different recipients. There were no differences in age or ovarian reserve parameters when analyzing the subgroups of donors producing none, one, two, or more pregnancies (data not shown).

Impact of Embryo Quality and Number of Embryos Transferred. There was a significant difference in clinical pregnancy and implantation rate according to the quality of embryos transferred. Optimal quality embryos (Score 1) resulted in the highest clinical pregnancy and implantation rate (50 and 29%, respectively); transfer of Score 2 and Score 3 embryos (moderate and lowest embryo qualities) resulted in 38 and 28% clinical pregnancy rates and 19 and 15% in implantation rate, respectively ($P < 0.05$, contingency table analysis).

There was no significant relationship between the number of embryos transferred (2, 3, or 4 embryos) and the clinical pregnancy rate ($P > 0.1$; contingency table analysis) (Fig. 4). However, increasing the number of embryos transferred was associated with an overall significantly enhanced multiple pregnancy rate ($P < 0.01$). Twin pregnancies were significantly higher when three or four embryos were transferred ($P < 0.05$). Although the occurrence of triplets was also higher when three or four embryos were

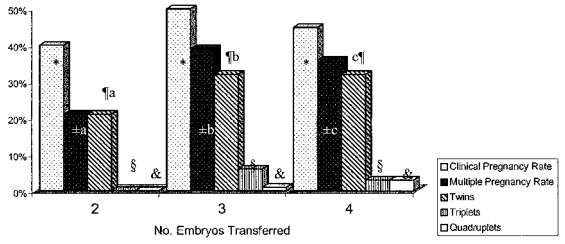

Fig. 4. Relationship between the number of embryos transfered and pregnancy and multiple pregnancy rates. * $P > 0.1$; ±a vs. ±b = $P < 0.05$; ±b vs. ±c = $P > 0.1$; ¶a vs. ¶b = $P < 0.05$; ¶b vs. ¶c = $P > 0.1$; § $P > 0.1$; & $P > 0.1$.

transferred, the difference was not significant (possibly because of the lower number of such pregnancies) (Fig. 4).

The difference in pregnancy rate between the elective transfer of two embryos (cases in which more than two embryos were available for transfer and two were selected judged upon morphology and cleavage criteria) and nonelective transfer of two embryos (cases in which only two embryos were available for transfer) was studied. In the elective two-embryo transfer group the clinical pregnancy rate was 45%, while in the nonelective two-embryo transfer group was the pregnancy rate was 27% ($P < 0.05$). Uterine transfer of two embryos resulted in the highest implantation rate (30%). There was a statistically significant difference when these results were compared with the transfer of three or four embryos (20 and 24%) ($P < 0.05$; contingency table analysis).

Recipients' Variables: Impact of Age and Endometrial Characteristics. The age of the recipients did not influence implantation, pregnancy, multiple pregnancy, or miscarriage rates ($P > 0.1$, data not shown). There was no significant relationship between the endometrial thickness and the clinical pregnancy rate or the live birth rate ($P > 0.1$). However, if a threshold of endometrial thickness was arbitrarily established at 8 mm, then a significant difference could be demonstrated. When the endometrial thickness was ≥8 mm, the pregnancy rate was 45%, whereas when the thickness was between <8 and ≥4 mm, the pregnancy rate was 17% ($P < 0.05$).

The distribution of patients according to the endometrial pattern was as follows: 90% of patients showed a trilaminar endometrial pattern (pattern B), while 11% exhibited a homogenous pattern (pattern A). There was no significant difference in pregnancy rate when comparing patients according to such patterns ($P > 0.1$)

DISCUSSION

This study performed on a relatively large cohort of oocyte donation patients was designed in order to fulfill two major aims: (i) to identify potential donor and recipient variables with impact on pregnancy outcome; and (ii) to identify statistically valid factors that allow us to establish policies to optimize pregnancy potential and to reduce the incidence of multiple births in this population.

This cohort of 146 healthy donors underwent 257 stimulation cycles accomplished with luteal phase GnRH agonist downregulation (long protocol using a dose of 0.5 mg/day reduced to 0.25 mg/day at menses) and recombinant FSH. Within this context, the age of the donors and individual parameters of the ovarian reserve demonstrated significant relationships with the observed response to controlled ovarian hyperstimulation.

The age of the donor was positively related to the total number of gonadotropin used. Basal cycle day 3 serum FSH levels were positively related to the number of gonadotropin ampoules used and to the number of mature oocytes retrieved. Our data indicated that there was an optimal FSH range between 4–8 IU/L associated with highest oocyte yield. It has to be kept in mind that such relationship is statistically significant even considering a relatively small range of FSH levels as oocyte donors are preselected with an FSH <10 IU/L. Although unexpected, this finding may indicate that normally cycling women with lower FSH levels (2–4 IU/L) may behave almost as subtle hypogonadal individuals in that they develop fewer follicles/oocytes upon gonadotropin stimulation (21). However, their pregnancy potential (i.e., egg quality) is not affected. On the other hand, individuals with higher FSH levels may demonstrate follicular development more typical to the one observed in low responders. These data need to be confirmed by future studies of a large pool of oocyte donors.

Neither donor's age and serum levels day 3 FSH, nor any parameters of the ovarian response), were significantly associated with implantation or pregnancy. We did observe, however, that basal cycle day 3 serum LH levels were associated with a higher occurrence of spontaneous miscarriages. When basal LH levels were >9 UI/L, there was a significantly enhanced risk for miscarriage (likelihood ratio of 4.3).

In a previous study of a population of women attempting pregnancy, subjects with an elevated serum LH experienced a miscarriage rate of 30–64% compared to 12% in women with normal LH levels (22).

Similarly, IVF patients with higher serum day 3 LH levels have also been shown to be at increased risk of miscarriage compared to patients undergoing IVF with normal serum day 3 LH levels (23). The mechanism(s)underlying the reported association of hypersecretion of LH with high incidence of miscarriages remains unclear. Several studies have suggested that an inappropriately high LH concentration in the follicular phase of the cycle may cause premature resumption of meiosis leading to the release of a prematurely aged oocyte. Such oocytes may be expected to produce embryos that have a poor developmental potential (24). Ludwig *et al.* also reported a high rate of miscarriage in patients with high serum LH levels undergoing IVF augmented with ICSI. In such study, as in ours, the patients had been downregulated with a GnRH agonist. These authors suggested that a chronic, long-term exposure of the oocytes to high LH concentrations might be the cause of impaired cytoplasmic maturity and the consequent miscarriage (25). It can be speculated that a longer pituitary suppression could be helpful in these patients.

We also found that basal cycle day 3 serum E_2 levels were independently and negatively associated with a significant decline in implantation rate. Basal cycle day 3 serum E_2 level was proposed as an accurate IVF outcome predictor by others (26–28). Licciardi *et al*. (26) showed a significantly lower pregnancy rate with increasing basal E_2 levels. Smotrich *et al*. (27) reported lower pregnancy and implantation rate with serum day 3 E_2 levels higher than 80 pg/mL. High levels of E_2 could be indicative of an intermediate stage of ovarian aging. In this stage lower levels of inhibin might result in a transiently elevated FSH. The FSH elevation might be followed by increasing production of E_2. This higher E_2 concentration feeds back centrally and to decrease FSH, resulting in higher E_2 levels but normal FSH.

For all other variables, no significant cut off value associated with clinical success could be demonstrated. Although there was no significant association between the number of mature oocytes retrieved and pregnancy or implantation, there was a clear trend for diminished conception rates when the number of oocytes was <6. As a consequence, it may be prudent to cancel donors during stimulation if this number of developing follicles is not observed.

Donors who were stimulated more than once had an overall pregnancy rate as high as 84%; such finding documents the fertility potential of the selection criteria. Donors who achieved a pregnancy were more consistent in demonstrating success in subsequent cycles. However, we could not identify any parameter (basal or related to ovarian response) that could predict the ability to conceive even within this selected group of successful donors. We did find, nevertheless, that consecutive stimulations were not harmful to ovarian response and that there was no demonstrable decrease in fertility potential associated with multiple stimulations. This finding is in agreement with previous reports (29,30).

The impact of the quality and number of transferred embryos on pregnancy outcome was expected. The transfer of embryos evidencing best morphological characteristics and advanced cleavage was significantly associated with higher pregnancy rates. In addition, the transfer of three or four embryos was associated with increased multiple pregnancy rates. Very importantly, we found that the transfer of two elective embryos resulted in high pregnancy rates (similar to the transfer of three embryos) and eliminated high order multiple pregnancies. It is our current policy to transfer two embryos electively on day 3 if embryos with ≥ 8 blastomeres having a morphological score of 1–2 are present in the cohort. Prospective, randomized studies are needed to determine if such policy yields favorable results as compared to blastocyst transfer.

Our results demonstrated unequivocally that the age of the recipient did not impact implantation or pregnancy outcome. Although there was no significant association between endometrial thickness and implantation, pregnancy outcome was improved in patients showing an endometrial lining thickness >8 mm. There have been controversial reports in this regard (31–35). We were unable to find a correlation between the ultrasonographic appearance of the endometrium (pattern) and pregnancy or implantation rates (32,35).

In conclusion, in this cohort of 146 young donors we could not identify statistically valid or conclusive associations of clinical success in oocyte donation. The heterogeneity of donor's basal characteristics and response to ovarian hyperstimulation appear to be the most important factors affecting the success of an oocyte donation cycle. We recognize the inherent biases associated with clinical retrospective studies such as this one. However, the results presented herein are derived from the assessment of a relatively large sample size analyzed using powerful statistical methods giving validity to the conclusions reached and to the formulation of clinical recommendations.

Although no single or combined donor or recipient variable(s) could be identified as predictor(s) of

pregnancy, the data suggest that donors ≤33 years of age with an ovarian reserve depicting a basal cycle day 3 serum FSH in the range of 4–8 IU/L, an LH <8 IU/L, and a basal E2 < 70 pg/mL had an optimal outcome. Using GnRH agonist suppression (long protocol, moderate downregulation) and recombinant FSH stimulation, the transfer of two selected embryos on day 3 yields a very favorable pregnancy outcome while significantly reducing the occurrence of multiple pregnancies. These policies, in addition to the implementation of embryo cryopreservation, resulted in a total reproductive potential of 60% and appears to maximize pregnancy outcome in oocyte donation.

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