

Donor age is paramount to success in oocyte donation*

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Several reports suggest increasing age in oocyte donors decreases the chances of in-vitro fertilization (IVF) success, while others describe no effect. The published data concerning gravidity and parity are similarly conflicting. To further address these questions, we retrospectively studied 445 consecutive donor IVF cycles at two large university-based IVF practices. Donor cycles were analysed for the number of oocytes retrieved, gravidity, parity, and age of the donor, and pregnancy outcome in recipients. The previous gravidity and parity of the donor were not associated with successful pregnancy in recipients. The number of oocytes retrieved was positively correlated with pregnancy. However, after adjusting for donor age, neither prior fertility nor the number of oocytes retrieved were significant predictors. In contrast, the donor's age was highly associated with recipient success. We conclude that the age of the oocyte donor is a significant predictor of pregnancy success and should be a major factor in selecting prospective candidates. The gravidity and parity of the donor are insignificant predictors, as are the total number of oocytes retrieved at the time of oocyte harvest.

Key words: age/gravidity/in-vitro fertilization/oocyte donor/parity

Introduction

Many studies have examined the effect of recipient age on donor in-vitro fertilization (IVF) outcome since it distinguishes whether the ageing egg or uterus determines the well-established age-related decline in female fertility (Rotsztein and Asch, 1991; Sauer *et al.*, 1992; Abdalla *et al.*, 1993; Yaron *et al.*, 1993; Flamigni *et al.*, 1993; Balmaceda *et al.*, 1994; Navot *et al.*, 1994; Legro *et al.*, 1995; Check *et al.*, 1995; Cano *et al.*, 1995; Levran *et al.*, 1996; Borini *et al.*, 1996; Remohí *et al.*, 1997; Stolwijk *et al.*, 1997). However, this has little clinical value to recipients

who do not use their own eggs. Of great interest to recipient couples are the personal characteristics of their egg donor. To date, there are only a few conflicting studies addressing whether donor age and prior donor fertility significantly influence pregnancy success. Furthermore, it has been suggested that increasing age in oocyte donors decreases the chances of recipient success (Rotsztein and Asch, 1991; Balmaceda *et al.*, 1994; Faber *et al.*, 1997). Others describe no effect (Abdalla *et al.*, 1993; Wong *et al.*, 1996; Stolwijk *et al.*, 1997). Published data concerning donor gravidity (Darder *et al.*, 1996; Faber *et al.*, 1997) and parity (Abdalla *et al.*, 1990; Rotsztein *et al.*, 1992) are similarly difficult to interpret.

We chose to address these questions using a large database to ascertain which variables (donor age, gravidity, parity, or the number of oocytes retrieved), if any, are important predictors of outcome. The database is unique since all donors were directed to individual recipients, and not shared. In addition, since only paid donors were utilized, all eggs were used for individual cycles, and the data were not biased by embryo selection or other confounding variables present when infertile women are used as donors.

Materials and methods

The protocol for oocyte donation was reviewed and approved by the institutional review boards of the respective medical centres. Oocyte donors underwent ovarian stimulation and transvaginal retrieval of oocytes as previously described (Sauer, 1995). A total of 621 consecutive donor cycles from 1991–1997 at two academic centres (University of Southern California and Columbia Presbyterian Medical Center) was analysed. Outcome parameters included the number of oocytes retrieved, the gravidity, parity, and age of the oocyte donor, and the ongoing pregnancy rate, defined as delivered or ongoing pregnancies past the first trimester; 176 cycles were excluded due to lack of documentation of any of the above parameters, leaving 445 cycles in this sample (286 from the University of Southern California and 166 from the Columbia Presbyterian Medical Centre). To detect any difference in pregnancy outcome due to age, the donors were divided into seven groups with 3 year intervals (group 1, aged 20–22 years; group 2, 23–25 years; group 3, 26–28 years; group 4, 29–31 years; group 5, 32–34 years; group 6, 35–37 years; group 7, aged >38 years).

Statistical analysis was performed using the SAS package (SAS Institute, Cary, NC, USA). The statistical significance of association was tested by Student's *t*-test for continuous data, and by the χ^2 test for nominal data. The strength of association was assessed by odds ratios. The multivariate logistical regression model was applied to calculate the odds ratios for donor age and pregnancy, with adjustment for gravidity, parity, and oocyte number at retrieval. $P < 0.05$ was considered to be statistically significant.

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Table I. Ongoing pregnancy rates versus donor gravidity, parity, and number of oocytes retrieved. Values are given as percentage means ± SD

	Pregnant (n = 170)	Not pregnant (n = 275)	Unadjusted P value ^a
G = 0	30.0 ± 3.5 (51)	19.6 ± 2.4 (54)	
G > 0	70.0 ± 3.5 (119)	80.4 ± 2.4 (221)	< 0.05
P = 0	47.1 ± 3.8 (80)	31.6 ± 2.8 (87)	
P > 0	52.9 ± 3.8 (90)	68.4 ± 2.8 (188)	< 0.05
No. of oocytes retrieved	16.5 ± 8.3	15.0 ± 7.7	< 0.05

G = gravidity; P = parity.

^aWhen adjusted by age, there were no significant differences.

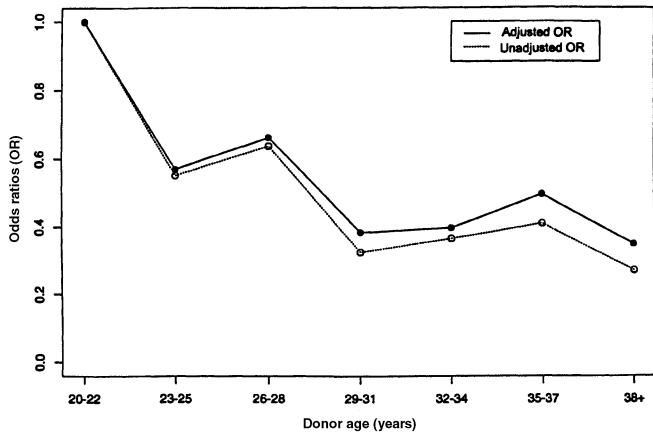


Figure 1. Odds ratios (OR) of donor age on ongoing pregnancy. Multivariate logistical regression model was applied to calculate the OR for donor age and ongoing pregnancy, with adjustment for gravidity, parity, and oocyte number at retrieval. There was no statistically significant difference between the adjusted and unadjusted OR.

Results

Mean donor age was 29.6 ± 5.1 years (range 20–41). The median donor gravidity was 2 (range 0–8). The median donor parity was 1 (range 0–5). Mean oocyte number was 15.6 ± 8.0, a median of 14 (range 2–57).

The donor’s previous gravidity and parity were negatively associated with pregnancy. After correcting for donor age, however, prior fertility was not a significant predictor of cycle outcome (Table I). Cycles resulting in pregnancies had a significantly higher number of retrieved oocytes. Once again, after correcting for donor age, the significance of oocyte number at retrieval on pregnancy disappeared (Table I).

On the other hand, donor age was highly associated with IVF success (P = 0.02). A comparison of the odds ratios of pregnancy with age alone versus age adjusted by gravidity, parity, and oocyte number shows remarkably similar values (not significantly different), indicating that age was the predominant predictor of pregnancy success (Figure 1). It is therefore sufficient to predict the probability of pregnancy by donor age alone.

Results of donor age versus ongoing pregnancy rate are given in Table II. A significant decline (>10%) in fertility appeared beginning at donor age 29 years, and another smaller decline at ages of >37 years. In donors aged <23 years, the ongoing pregnancy rate was 59.1%, and in those aged 23–28

years the ongoing pregnancy rate ranged from 42.4 to 45.9%. Donors aged 29–37 years had significantly lower ongoing pregnancy rate ranging from 30.5 to 34.9%, although after the initial decline the ongoing pregnancy rate remained fairly constant in the low to mid 30s. A further drop-off to an ongoing pregnancy rate of 27.3% was noted in patients aged >37 years, although this drop was of smaller magnitude than that seen at age 29 years.

All of the above statistical evaluations were also analysed for any differences that could be attributed to the site of the cycle (University of Southern California and Columbia Presbyterian Medical Center). The site of the cycle was not a significant predictor of cycle outcome.

Discussion

We have found that the age of the oocyte donor is of paramount importance in predicting pregnancy outcome, while donor gravidity, parity, and the number of oocytes retrieved are insignificant once controlled for donor age.

Previous studies have shown a positive effect of younger donor age on IVF outcome. Balmaceda *et al.* evaluated 258 donor cycles and found a significant decline in the pregnancy rate at ages of >35 years, although the statistical significance disappeared after logistic regression analysis (Balmaceda *et al.*, 1994). Rotsztejn and Asch studied 108 donor cycles; they divided the donors into their 20s and 30s and found a significantly higher clinical pregnancy rate in the younger group (Rotsztejn and Asch, 1991). Faber *et al.* appraised 568 donor cycles and noted a significant decline in both clinical and delivered pregnancy rate in donors aged ≥33 years (26.6 and 22.1% compared with 43.5 and 35.1% respectively), and suggested that donors aged >32 years could be excluded from donor programmes (Faber *et al.*, 1997).

Several studies have not found a significant effect of donor age on IVF outcome. Donor age was positively associated with pregnancy rate in 100 cycles (Abdalla *et al.*, 1990). In a continuation of their series, these authors (Abdalla *et al.*, 1993) evaluated 371 donor cycles and found no effect of donor age on clinical pregnancy rate up to and including age 39, although an increase in miscarriage was noted in cycles employing older donors. While donor age was equivalent in both successful and unsuccessful cycles, no evaluation of separate age categories was performed. Similarly, this study is a continuation of series (Wong *et al.*, 1996; Stolwijk *et al.*, 1997) that found different results based upon an expanding database. Wong *et al.* divided 458 donor cycles from 1988–1995 into two groups: one in their 20s and the other in their 30s (Wong *et al.*, 1996). The younger group had more oocytes per retrieval, but no benefit was noted in either clinical or delivered pregnancy rate. Even when donor age was split into 5 year categories, no evidence of an age effect was present. They did not control for donor gravidity, parity, or number of oocytes. The second study (Stolwijk *et al.*, 1997) was limited to include only the first recipient cycle, but reached the same conclusions. They evaluated 294 donor cycles from 1991–1995 and also found a decrease in oocytes retrieved with advancing donor age. After sorting the donors by 5 year intervals they found no effect of

Table II. Ongoing pregnancy rates versus donor age

Group	1	2	3	4	5	6	7
Age (years)	20–22	23–25	26–28	29–31	32–34	35–37	38+
Number (n)	44	66	74	82	94	63	22
Pregnancy rate	59.1	42.4	45.9	30.5 ^a	30.9 ^a	34.9 ^a	27.3 ^a
SD	±7.3	±6.0	± 5.7	±5.0	±4.8	±6.0	±9.1

^aP < 0.05 compared with groups 1, 2 and 3.

Pregnancy rate includes only delivered pregnancies or pregnancies ongoing past the first trimester.

donor age on pregnancy rate. The present study used an expanded data set of 621 donor cycles from 1991–1997. As mentioned earlier, we excluded cycles for which data was missing on any of the variables studied, leaving 445 of 621 cycles for evaluation. The series reported earlier had a bell-shaped curve for donor age, while the current study has a more even age distribution, enabling a more accurate interpretation at the age extremes. Furthermore, we divided the cycles into seven groups by 3 year intervals, again increasing the statistical accuracy. We found that the younger donors had a significant benefit on pregnancy rate, even after controlling for prior donor fertility, number of oocytes, and the site of the cycle.

The effect of donor gravidity and parity in this study suggests that prior fertility is adversely associated with pregnancy outcome (Table I). Corrected for donor age, however, the effect of previous donor fertility became insignificant.

Faber *et al.* evaluated 185 cycles for the effect of donor gravidity and came to the same conclusion (Faber *et al.*, 1997). In contrast, another study (Darder *et al.*, 1996) included only 64 cycles and found that prior donor gravidity was positively associated with pregnancy outcome. This result may be an artefact of small sample size. In addition, Rotsztein *et al.* evaluated donor parity in 83 regular donor cycles and concluded that it was an insignificant predictor of outcome (Rotsztein *et al.*, 1992). The first study by Abdalla *et al.* reported donor parity in 100 cycles and found that prior donor parity and younger donor age were both positively associated with pregnancy rate in that sample (Abdalla *et al.*, 1990). However, when they increased their sample size by nearly four times in a later study, their conclusions regarding donor age were reversed (Abdalla *et al.*, 1993).

We did not control for recipient age, but most large series evaluating recipient age have demonstrated no effect (Rotsztein and Asch, 1991; Sauer *et al.*, 1992; Abdalla *et al.*, 1993; Balmaceda *et al.*, 1994; Navot *et al.*, 1994; Check *et al.*, 1995; Legro *et al.*, 1995; Remohí *et al.*, 1997; Stolwijk *et al.*, 1997). A smaller number of papers suggest an adverse effect of advanced recipient age (Yaron *et al.*, 1993; Flamigni *et al.*, 1993; Cano *et al.*, 1995; Borini *et al.*, 1996; Levran *et al.*, 1996); some of these used subfertile women (women undergoing IVF themselves who donated their excess oocytes) as donors (Yaron *et al.*, 1993; Levran *et al.*, 1996). Recipient age most likely did not confound our results and was certainly less significant in proportion to the effect of the ageing oocyte donor. Similarly, we did not control for paternal age. Other authors (Gallardo *et al.*, 1996) found no significance of paternal age on outcome of oocyte donation through to age 64 years.

In summary, we suggest younger donors provide higher chances for pregnancy in recipients but we do not recommend a firm upper-age limit. Rather, we believe a recipient couple should be informed of donor age as one characteristic among others, such as physical appearance, to consider in choosing an appropriate donor. Although a 35 year old donor is not as fecund as a 21 year old, her physical traits or ethnic background may nonetheless make her a more desirable choice for some. We do not consider the drop-off in pregnancy rates, ~25–30%, so overwhelmingly significant as to constitute an absolute contraindication to the use of oocytes from older donors. Prior fertility, on the other hand, is not a significant donor attribute.

References

- Abdalla, H.I., Baber, R., Kirkland, A. *et al.* (1990) A report on 100 cycles of oocyte donation; factors affecting the outcome. *Hum. Reprod.*, **5**, 1018–1022.
- Abdalla, H.I., Burton, G., Kirkland, A. *et al.* (1993) Age, pregnancy, and miscarriage: uterine versus ovarian factors. *Hum. Reprod.*, **8**, 1512–1517.
- Balmaceda, J.P., Bernadini, L., Ciuffardi, I. *et al.* (1994) Oocyte donation in humans: a model to study the effect of age on embryo implantation rate. *Hum. Reprod.*, **9**, 2160–2163.
- Borini, A., Bianchi, L., Violini, F. *et al.* (1996) Oocyte donation program: pregnancy and implantation rates in women of different ages sharing oocytes from single donor. *Fertil. Steril.*, **65**, 94–97.
- Cano, F., Simón, C., Remohí, J. and Pellicer, A. (1995) Effect of ageing on the female reproductive system: evidence for a role of uterine senescence in the decline in female fecundity. *Fertil. Steril.*, **64**, 584–589.
- Check, J.H., O'Shaughnessy, A., Lurie, D. *et al.* (1995) Evaluation of the mechanism for higher pregnancy rates in donor oocyte recipients by comparison of fresh with frozen embryo transfer pregnancy rates in a shared oocyte programme. *Hum. Reprod.*, **10**, 3022–3027.
- Darder, M.C., Epstein, Y.M., Treiser, S.L. *et al.* (1996) The effects of prior gravidity on the outcomes of ovum donor and own oocyte cycles. *Fertil. Steril.*, **65**, 578–582.
- Faber, B.M., Mercan, R., Hamacher, P. *et al.* (1997) The impact of an egg donor's age and her prior fertility on recipient pregnancy outcome. *Fertil. Steril.*, **68**, 370–372.
- Flamigni, C., Borini, A., Violini, F. *et al.* (1993) Oocyte donation: comparison between recipients from different age groups. *Hum. Reprod.*, **8**, 2088–2092.
- Gallardo, E., Simón, C., Levy, M. *et al.* (1996) Effect of age on sperm fertility potential: oocyte donation as a model. *Fertil. Steril.*, **66**, 260–264.
- Legro, R.S., Wong, I.L., Paulson, R.J. *et al.* (1995) Recipient's age does not adversely affect pregnancy outcome after oocyte donation. *Am. J. Obstet. Gynecol.*, **172**, 96–100.
- Levran, D., Goldstein, I., Dor, J. *et al.* (1996) Parameters that influence the results of *in vitro* fertilization/embryo transfer: a study of an egg donation model. *Gynecol. Endocrinol.*, **10**, 401–406.
- Navot, D., Drews, M.R., Bergh, P.A. *et al.* (1994) Age-related decline in female fertility is not due to diminished capacity of the uterus to sustain embryo implantation. *Fertil. Steril.*, **61**, 97–101.
- Remohí, J., Gartner, B., Gallardo, E. *et al.* (1997) Pregnancy and birth rates after oocyte donation. *Fertil. Steril.*, **67**, 717–723.
- Rotsztein, D.A. and Asch, R.H. (1991) Effect of ageing on assisted reproductive technologies (ART): experience from egg donation. *Sem. Reprod. Endocrinol.*, **9**, 272–279.

- Rotsztejn, D.A., Ord, T., Balmaceda, J.P. and Asch, R.H. (1992) Variables which influence the selection of an egg donor. *Hum. Reprod.*, **7**, 59–62.
- Sauer, M.V. (1995) Oocyte donation; reviewing a decade of growth and development. *Sem. Reprod. Endocrinol.*, **13**, 79–84.
- Sauer, M.V., Paulson, R.J. and Lobo, R.A. (1992) Reversing the natural decline in human fertility. *J. Am. Med. Assoc.*, **268**, 1275–1279.
- Stolwijk, A.M., Zielhuis, G.A., Sauer, M.V. *et al.* (1997) The impact of the woman's age on the success of standard and donor *in vitro* fertilization. *Fertil. Steril.*, **67**, 702–710.
- Wong, I.L., Legro, R.S., Lindheim, S.R. *et al.* (1996) Efficacy of oocytes donated by older women in an oocyte donation programme. *Hum. Reprod.*, **11**, 820–823.
- Yaron, Y., Botchan, A., Amit, A. *et al.* (1993) Endometrial receptivity: the age-related decline in pregnancy rates and the effect of ovarian function. *Fertil. Steril.*, **60**, 314–318.

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