

## Comparison of Pregnancy Rates Following in Vitro Fertilization–Embryo Transfer Between the Donors and the Recipients in a Donor Oocyte Program

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*Our in vitro fertilization (IVF) program provides a unique opportunity to evaluate influences of hormonal milieu on pregnancy outcome, by using a shared pool of oocytes obtained by donors (in exchange for financial assistance). The study presented herein evaluated 38 retrieval cycles (28 oocyte donors/22 recipients). No difference in mean number of embryos transferred was seen (2.7 in the donors vs 2.8 in the recipients). However, a statistically significant difference was seen in the pregnancy rates per retrieval (10.5% donors vs 29% recipients) and per transfer (4/35, 11.1%, vs 11/34, 32.3%). Abortion rates were similar (25% donor, 27.2% recipients). These data suggest that other reports of higher pregnancy rates from donor oocyte programs may not be due exclusively to better-quality oocytes. Possibly a negative effect of hyperstimulation or adverse endometrial environment of the donor (possible chronic endometritis) may explain these data.*

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**KEY WORDS:** donor oocyte; recipients; hyperstimulation regimen; pregnancy rates.

### INTRODUCTION

The pregnancy rates at several centers reporting their data from donor oocyte programs have been even higher than the usual pregnancy rates which

occur following in vitro fertilization (IVF)–embryo transfer (ET). Some recently published reports include those from the Cleveland Clinic (33%) (1), the Centre for Reproductive Medicine, Brussels (30%) (2), and the IVF program in Kfar Saba, Israel (56%) (3). It may be that the higher pregnancy rates in the donor oocyte programs are related primarily to the use of oocytes from known highly fertile donors, whereas the pregnancy rates in conventional IVF-ET patients are somewhat reduced because patients undergoing the procedure may have an infertility problem related not only to damaged fallopian tubes but also to problems with oocyte quality.

Recent data from the University of California, Irvine (4), using a “shared” oocyte program, suggest that the improved pregnancy rates may be related more to differences in therapy (estrogen–progesterone replacement in the recipients versus hyperstimulation treatment in the donors) since the same pool of oocytes resulted in a 58% pregnancy rate (11/19) in the recipients versus only 37.5% (3/8) in the donors following gamete intrafallopian transfer (GIFT).

The present study was aimed at comparing the pregnancy rate of IVF-ET in donors versus recipients where the exclusive source of oocytes was the donors themselves. The objective was to see if the hyperstimulation regimen or the retrieval process may have a deleterious effect on the success of IVF. Finally, a comparison of endometrial biopsies in these two groups was made to see which therapeutic regimen is more apt to be associated with luteal-phase defects and whether this affects the pregnancy and abortion rate.

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## MATERIALS AND METHODS

Twenty-eight females undergoing IVF-ET were willing to share oocytes with females in ovarian failure in exchange for the recipients' sharing the costs of the procedure. The 28 donor females shared oocytes with 22 recipients in 38 cycles. Since the objective of the study was to compare pregnancy rates in donors versus recipients, no one was chosen for a donor who had a male-factor problem. Thus all donors had either tubal-factor ( $n = 32$ ) or unexplained ( $n = 6$ ) infertility. All donors were 38 or younger. All 22 recipients had ovarian failure and their ages ranged from 26 to 46.

The controlled hyperstimulation regimen employed has been described by Meldrum *et al.* (5). The recipients were treated with replacement estrogen (estradiol orally, 2 mg), beginning on day 6 of the donor's leuprolide therapy, with an increment of 2 mg every 4 days up to 6 mg. The estrogen was increased to 8 mg when the donor received human chorionic gonadotropin (hCG), and progesterone (P), 50 mg im daily, was also started that day. Endometrial biopsies in the late luteal phase were performed in the first cycle of all patients not conceiving. An hCG beta-subunit level was obtained in the morning, and if it was negative, the biopsy was performed that evening. If it was slightly positive, then the hCG was repeated the next day, and if the levels were dropping, then a biopsy was performed that evening. The endometrial biopsies were all processed by Damon Clinical Laboratory (Trevose, PA) and were interpreted by their pathologists. A repeat endometrial biopsy was obtained in the second nonpregnancy cycle if the first was out of phase; if this occurred, an additional 25 mg progesterone per day was given above that given in the preceding cycle. The day of ovulation in the recipients used for calculation of the endometrial biopsies was assumed to be 2 days prior to embryo transfer. Pregnancy rates between the donors and the recipients were recorded and compared.

The donors and recipients were advised that the oocytes would be equally divided as well as possible according to number and quality. The donors were advised that, due to their donating half their oocytes, there would definitely be less possibility of having cryopreserved embryos replaced in subsequent cycles and possibly a reduced chance of conception related to the replacement of fewer embryos. Each recipient was taken according to time of registering. She was given a detailed description

of a donor (both physical characteristics and schooling) and she had the right to accept this donor or pass her on to the next recipient and be next in line again. Identities were kept confidential. Because of the investigational nature of the study, the charge for retrieval and transfer was reduced to \$800 and was paid by the recipient, who also supplied the medication.

## RESULTS

A comparison of pregnancy rates between donors and recipients is given in Table I. A threefold increased pregnancy rate per retrieval was seen in the recipients (11/38, or 29%) versus the donors (4/38, or 10.5%) ( $P = 0.04$ , Fisher's exact test). In three donor cycles no embryos were transferred, compared to four recipient cycles. Thus there were 11 pregnancies in 34 transfer cycles in recipients (32.3%) versus 4 pregnancies in 35 transfer cycles (11.1%) in donors ( $P = 0.03$ , Fisher's exact test). The abortion rates were similar (27.2% for recipients vs 25% for donors). An additional pregnancy in a donor was lost (ectopic) so that the ongoing pregnancy rate per retrieval cycle was 21% (8/38) in the recipients, compared to only 5.2% (2/38) in the donors ( $P = 0.04$ , Fisher's exact test). One of the recipients considered a failure in this study did conceive in her next cycle, following the transfer of two cryopreserved embryos that had resulted from the retrieval from the failed cycle (pregnancy is ongoing in the second trimester). The discordance in pregnancy rates is not explainable by differences in the number of embryos replaced (2.7 for donors, 2.8 for recipients); the quality of embryos transferred was also equal.

Endometrial biopsies were performed in 26 donors and 16 recipients the first cycle and in 8 donors and 9 recipients the second cycle. The endometrium

Table I. Comparison of Pregnancy Rates Between Oocyte Recipients and Oocyte Donors in Our IVF Program

	Stimulation cycles	Number of		
		Pregnancies	Spontaneous abortions	Ectopics
Recipients ( $n = 22$ )	38	11 (29%)	3	0
Donors ( $n = 28$ )	38	4 (10.5%)	1	1

dated in phase in 28 of 34 (82%) donor cycles versus only 10 of 25 (40%) recipient cycles.

Four of the eight nonaborted pregnancies in recipients resulted in successful deliveries including a set of twins; four others are in their last trimester. One of the donor pregnancies delivered successfully and the other is in the last trimester. All three of the recipients who aborted tried again; two of three were successful in the next attempt and both have single viable fetuses in the second trimester. The average age of the pregnant recipients was 36.8, ranging from age 26 to 46; the nonpregnant recipients ranged in age from 24 to 44 (mean, 36.3), and the nonpregnant donors from 26 to 39 (mean, 31.7). The oldest recipient to conceive was 46 and she delivered a healthy female; two others were 45 and 44, respectively, and have successfully completed the second trimester.

## DISCUSSION

Most centers with a donor oocyte program are reporting a higher pregnancy rate in the recipients than in the general IVF-ET program. A possible explanation for these findings is the selection of fertile donors. The data presented herein, however, demonstrate an approximately threefold greater pregnancy rate in the recipients than the donors, despite the replacement of almost exactly the same number of embryos in both. This discordance is even more interesting when one considers that the large majority of the donors was in the group which normally has the highest pregnancy rates—tubal-factor problems. Thus we corroborate the conclusions reached by Borrero *et al.* in comparing GIFT in donors and recipients (4).

The data suggest that the hyperstimulation regimen or ovarian trauma by follicular puncture may have a negative effect on the success of the procedure. Alternatively, possibly the use of estrogen in the luteal phase in the recipients is responsible in some way for the improved pregnancy rate. The pregnancy rate per transfer (11.1%) in the donors was just slightly lower than the 13.6% rate reported to SART for Endocrine Histology's 1989 statistics.

This might be related to the decreased number of embryos transferred related to sharing oocytes.

It is not clear why the conception rate in the recipients was so high considering the high incidence of luteal-phase deficiencies (LPD). The rising hCG levels may stimulate the corpus luteum and correct the endometrium in the donors but there is no corpus luteum to stimulate in the recipients. Borrero *et al.*, who demonstrated a 58% pregnancy rate in recipients, stated that 100% of these patients' biopsies were out of phase (4). We considered a biopsy out of phase only if it was more than 2 days early for dates, and they called it abnormal if it was 2 days out of phase; so if they used our system 50% of the recipients would have luteal-phase deficiencies and 50% would be abnormal with late luteal-phase biopsies. It should be noted that none of the patients had prior cycles of estrogen and progesterone replacement without embryo transfer in an effort to adjust the endometrial biopsy to be in-phase.

The successful pregnancies achieved in three women aged 44–46 in four transfer cycles total raise questions concerning the significance of the uterine senescent factor as a cause of the poor IVF success rate in women over 40 years of age.

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