FACTORS AFFECTING THE OUTCOME OF OOCYTE DONATION CYCLES

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Abstract- The success of oocyte donation is influenced by multiple factors. We performed a retrospective analysis to evaluate prognostic factors in oocyte donation cycles. The main outcome measurements including recipient age, donor age, estradiol level in midcycle, the day of transfer and number of transferred embryos were not different in pregnant and non pregnant groups. Endometrial pattern but not endometrial thickness was useful in predicting pregnancy outcome. Clinical pregnancy rates were not different relative to etiology of infertility. Clinical pregnancy rates in poor responders and patients with ovarian failure were 23.8% and 26.7%, respectively. Clinical pregnancy rate for zygote intrafallopian transfer (ZIFT) and rapid ZIFT was 31% vs 11.1% for uterine embryo transfer. Predictive factors for pregnancy in oocyte donation cycle were endometrial pattern and route of transfer (ZIFT and rapid ZIFT).

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INTRODUCTION

There are numerous studies concerning pregnancy rates in oocyte donation cycles. The success of oocyte donation is influenced by multiple factors including the age of the oocyte donor and recipient, the quality of embryo and the reproductive status and endometrial receptivity of the recipient (1).

Among these factors donor age is the most important factor in in-vitro fertilization (IVF) outcome (2). The relation between recipient age and success of oocyte donation cycle is controversial (2-4). Both endometrial thickness (5) and pattern (6) have been implicated as predictors for success in oocyte donation. The route of transfer (zygote intrafallopian transfer [ZIFT] or uterine embryo transfer [UET]) and its effect on outcome of donation cycle remains a controversy. No significant difference was observed when ZIFT was applied as opposed to UET in one study (7) but in another study the pregnancy rate was significantly higher with ZIFT compared to UET (8).

The purpose of the present study was to determine the factors affecting the outcome of oocyte donation cycles.

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MATERIALS AND METHODS

We evaluated retrospectively all oocyte donation cycles (n = 114) from January 1999 through December 2001. All donors were anonymous (19-34 years). Every recipient underwent a preprocedure laboratory test and hysterogram. Every donor underwent preprocedure hormonal assay, screening for HBsAg, HIV Ab and HCV Ab.

Oocyte donors and ovulatory recipients were down-regulated with high dose oral contraceptives (OCP) from follicular phase of previous cycle. On day 21 of the cycle, the OCP was discontinued and both donor and recipients were given a subcutaneous dose of 500 µg/d buserelin. In donors, in third day of menses human menopausal gonadotropin (HMG, 150-300 IU/d) was administered, accompanied by a

decrease in dose of buserelin (250 µg/d). In ovulatory recipients, oral estrogen was started at the beginning of their menstrual cycle and they were maintained on estrogen. The dose of buserelin was decreased to 250 µg/d too. In donors a daily dose of HMG was adjusted with vaginal sonographic monitoring. When at least two follicles reached 18 mm in diameter, 10000 IU of HCG was administered, and retrieval of oocyte was achieved after 34-36 hours.

In recipients, oral estrogen conjugate (0.625 mg/d) was begun at a dosage of 1 tab/day for 3 days, then increased one tab/day every 48 h to a maximum of 6 tab/day according to sonographic appearance. On the day of donors hCG injection, the recipients medications were adjusted as follows: GnRH was discontinued, 800 mg/day progesterone was administered transvaginally and conjugated estrogen was continued (2.5 mg/d). Non cycling recipients were administered estrogen with the same protocol, several days prior to initiating ovarian stimulation in the donor.

The route of transfer was ZIFT and rapid ZIFT in 87 (76%) patients and UET in 27 (24%) patients. In ZIFT group the transfer of two pronucleus zygotes was performed 24 h after oocyte retrieval whereas in rapid ZIFT it was done as soon as intra cytoplasmic sperm injection (ICSI) was performed. Tubal transfer was performed on the same day of retrieval.

In UET, embryos with 4-8 cells and grade 1or 2 were transferred on day 3 after oocyte retrieval. Estrogen and progesterone supplementation was continued until a negative pregnancy test or for 12 weeks if a pregnancy had resulted. Clinical pregnancy was defined as a gestational sac visualized on vaginal sonography.

Data were evaluated by X^2 analysis and Fisher exact test with comparative significance determined at $P< 0.05$.

RESULTS

The clinical pregnancy was seen in 30 out of 114 (26.3%) and all of them were singleton pregnancies. The mean age of recipients was 37.5 ± 4.8 (28-45 years). There was no significant difference between mean age of recipient in groups with clinical pregnancy and no clinical pregnancy (36.3 ± 4.8 v/s 38 ± 4.8, $P = 0.46$) (Table 1).

Table 1. Comparison of some parameters according to outcome of oocyte donation cycles

Parameter	Clinical pregnancy	No clinical pregnancy
Recipient age (years)	36.3±4.8	38±4.8
Donor age (years)	26.3±4.2	26.9±3.5
Mean estradiol (pg/ml)	1984±849	1998±840
Endometrial thickness (mm)	8±1.8	8.7±2.5
The day of transfer	15±2.5	16.1±1.9
Embryo number for transfer	5.9±2.6	4.5±2.6

*Data are given as mean± SD.

The mean age of donors was 26.7 ± 3.6 years (19-34). There was no significant difference in donors age between pregnant and non pregnant recipients (26.3 ± 4.2 vs 26.9 ± 3.5, $P= 0.92$).

In evaluating relationship between clinical pregnancy and etiology of infertility, clinical pregnancy occurred in 15 out of 63 women who were poor responders (23.8%), in 12 out of 45 women with ovarian failure (26.7%) and in 3 out of 6 women with surgical menopause. The difference between poor responders and patients with ovarian failure was not significant ($P > 0.05$) (Table 2).

The mean estradiol concentration in midcycle was 1984 ± 849 pg/ml (633-3084) with no significant difference between pregnant and non pregnant women.

The mean midcycle endometrial thickness of all recipients was 8.5 ± 2.3 mm (4-15 mm). There was no significant differences between pregnant and non pregnant women (8±1.8 vs 8.7±2.5, $P = 0.41$)

The endometrial pattern was triple line in 18 (23%), intermediate in 51 (65%) and solid in 9 (12%) (endometrial pattern was reported in 78 women). In recipients, pregnancy was achieved in 9 out of 18 women with triple line pattern (50%), in 9 out of 51 women with intermediate pattern (17.6%) and in none of women with solid pattern ($P<0.05$) (Table 2).

The day of transfer was on 15.8±2 day (13- 20) of cycle. The difference between pregnant and non pregnant group was not significant (15 ± 2.5 vs 16.1 ± 1.9 day of cycle). The mean number of embryos for transfer was 5.9 ± 2.6 in pregnant women versus 4.5 ± 2.6 in nonpregnant women that was not significantly different.

Table 2. Clinical pregnancy rate relative to ART techniques, endometrial pattern and etiology of infertility

Parameter	Clinical pregnancy	No clinical pregnancy	Pregnancy rate
ART technique			
Rapid ZIFT	18	39	31.6%
ZIFT	9	21	30%
ZIFT and rapid ZIFT	27	60	31.0 %
UET	3	24	11.1 %
Endometrial pattern			
triple line	9	9	50%
Intermediate	9	42	17.6%
Solid	0	9	0%
Etiology of infertility			
Poor responder	15	48	23.8%
Ovarian failure	12	33	26.1%
Surgical menopause	3	3	50%

Abbreviations: ART, assisted reproductive technique; ZIFT, zygote intrafallopian transfer; UET, uterine embryo transfer.

In evaluating relation between clinical pregnancy and assisted reproductive techniques, 27 clinical pregnancies occurred in 87 tubal transfers (ZIFT and rapid ZIFT, 31%) and three clinical pregnancies occurred in 27 UET (11.1%). This difference was significant ($P < 0.05$) (Table 2).

DISCUSSION

Among prognostic factors for pregnancy in donation cycles, endometrial pattern and route of transfer were significantly different between pregnant and non pregnant women ($P < 0.05$). Endometrial pattern has been reported to be somewhat predictive of pregnancy outcome in conventional IVF cycles and specifically lower pregnancy rates have been noted in cycles where the solid endometrial configuration is exhibited (9). Study of Noyes *et al.* suggested that the three observed endometrial patterns of prepared cycles had equal probability for positive pregnancy outcome (10). Clinical pregnancy rates in ring (triple line), intermediate and solid patterns were 64%, 52% and 69%, respectively. The current data suggest that in triple line pattern of endometrium, the chance of positive pregnancy outcome is increased. These data show the importance of sonographic monitoring of endometrium in recipient and fine adjustment of estrogen dose for better development of endometrium.

There are several additional theoretical advantages of ZIFT over UET, for example further development of embryo before entry to uterine cavity. The presence of numerous growth factors and cytokines in the human tubal fluid may contribute to the development of the early embryo and may enhance implantation. In this study we find out that tubal environment is more suitable for development of embryo of donor oocyte too. Scott *et al.* showed that oocyte quality and pronuclear embryo morphology are related to implantation and that pronuclear embryos can be successfully selected for embryo transfer (11). In study of Pados *et al.*, clinical pregnancy rate was 27.5% in ZIFT as opposed to 19.6% in UET; the difference was not significant but the trend to pregnancy was higher in ZIFT (7). In our study clinical pregnancy in ZIFT was 31% vs 11.1% in UET ($P < 0.05$).

The recipients' ovarian status and requirement of GnRH agonist down regulation does not appear to influence on the outcome of an oocyte donation cycle. In Pados *et al.* study, ovarian function was not found to be of significant importance to the achievement of pregnancy after oocyte donation (7). In our study the difference of clinical pregnancy between poor responders and women with ovarian failure was not significant too.

We excluded all chemical and ectopic pregnancies. In our study, clinical pregnancy rate in ZIFT was 31% vs 11.1% in UET ($P < 0.05$) and in study of Pados *et al.* it was 27.5% vs 19.6%. So clinical pregnancy rate in our ZIFT group was the same as Pados'. In our study clinical pregnancy in UET was 11.1% and in Pados' was 19.5%. This low rate of clinical pregnancy may be due to our IVF laboratory conditions because other variables were same.

Donor oocytes are being used more and more. Defining prognostic factors for pregnancy can help to recruits appropriate candidates for this technique and

the best approach for recipients. Prospective clinical trial is needed for precise evaluation of predicting useful factors in the success of oocyte donation.

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