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The pivotal role of the number of transferred embryos in oocyte donation cycles: A retrospective cohort study

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Abstract

This research aimed to show the role of the number of transferred embryos on pregnancy outcomes of the oocyte donation cycles (ODC). This retrospective cohort study included 122 ODCs performed at a private in vitro fertilization (IVF) center between 2020 June - 2021 January. Cases with severe male infertility, tuboperitoneal, and endometrial factors were not included in the study. The median (interquartile range) recipient age was 43 (30–54) years. ODC results revealed that 10.7% of the cases were negative, 4.9% were biochemical pregnancies, and 84.4% were clinical pregnancies. Pregnancy outcomes were checked; miscarriage, preterm, and term delivery rates were 5.7%, 3.9%, and 90.4%, respectively. The rate of recipients for the younger than 40 years was 32%, between the 40–44 years was 27%, and between 45–54 years was 41% respectively. Statistically significant difference was not observed between age groups in terms of endometrial thickness ($p = 0.059$), number of transferred embryos ($p = 0.857$), number of ODC attempt ($p = 0.666$), live birth rate ($p = 0.1$), and other pregnancy outcomes ($p > 0.05$, for all). A total of 96 (78.7%) embryo transfers (ET) resulted in a live birth. In 8.2% (n=10) of cases, single embryo transfer (SET) and in 91.8% (n=112) of cases, double embryo transfer (DET) was performed. The number of embryos transferred was statistically significantly higher among cases that resulted in live births compared to cases without live births ($p = 0.002$). Significant difference was not found in terms of the recipient age ($p = 0.392$), male age ($p = 0.108$), endometrial thickness ($p = 0.478$), and the number of attempt ($p = 0.777$) between cases resulted in live birth or not. The only parameter that affects the live birth rates in ODC is the number of transferred embryos.

Keywords: Oocyte donation cycle, live birth rate, pregnancy outcome, number of transferred embryos

1. Introduction

Since the first successful IVF pregnancy was succeeded via donor oocytes in the 1980s, oocyte donation cycles (ODC) have been increasingly preferred among women who cannot conceive with their oocyte or when it is inconvenient to become pregnant with their oocyte (1). Although ODC is routinely used, it is also discussed at ethical tables, in religious settings, and in medical debates. Couples may apply to ODC for reasons such as decreased ovarian reserve due to advanced age or premature ovarian failure, hypergonadotropic hypogonadism, severe genetic diseases, and recurrent pregnancy losses (1,2). Donor age had to be used to determine the appropriate number of embryos to be transferred in ODCs (3). Moreover, a single high-quality blastocyst transfer is recommended to minimize multiple pregnancies and related complications in ODCs (3). Although using healthy and high-quality oocytes as much as possible is principal in ODC, some characteristics of the recipient woman and her husband affect the probability of successful pregnancy results. Many parameters such as the sperm quality used in fertilization, age of the recipient mother, body mass index (BMI), genetic characteristics, endometrial thickness, and pattern were associated with clinical outcomes in ODC (4-7). Single embryo transfer (SET) is recommended to avoid complications related to multiple pregnancies and to increase the live birth rate. However, specialists generally choose to transfer double embryos when they have a suspicion about the quality of embryos. Still, conventional morphological grading, which determines the embryo quality has limitations for predicting the live birth rates (8). In this research, it is expected to underline the effects of the number of transferred embryos predicting live birth rates in fresh ODC of couples with no

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embryos to be frozen.

2. Materials and methods

This retrospective cohort study included 122 ODCs conducted at a private IVF center in Cyprus. Data has collected between June 2020 and January 2021. Egg donors were 22 to 30 years old, and recipients were 30 to 54 years old. All patients were informed and signed a written consent form to share the results of treatment and to use data for research purposes in the academic area. The local Institutional Review Board (2020-10/1) has approved to do research for this study. Each patient was analyzed only once in this study.

2.1. Patients

Inclusion criteria

- Fresh donor oocytes were used in all ODC
- Couples without severe male factor or endometrial factor
- Donors aged between 22-30 years
- Recipient age <55 years
- Couples with no embryos to be frozen

Exclusion criteria

- Recipients with known endocrinologic problems and other chronic illnesses
- Donors with known genetic problems, endocrinologic problems, and other chronic illnesses
- Multiple pregnancies

2.2. Procedure

In cases where a decision was made for an ODC, 2 mg estradiol (E2) hemihydrate (17beta-estradiol) treatment was started orally three times a day and was continued at the same dose for at least 7 days. The dose was increased (2× 2 per oral per day) in cases of thin endometrium (< 7mm) or serum E2 did not reach 300 pg/ml. Simultaneously with ovulation trigger in donor women, intramuscular progesterone injection 1x100mg per day was started in the recipient women. Estradiol and progesterone were administered together after embryo transfer. These medications had been used until a βhCG test. Controlled ovarian stimulation for egg donors was done by recombinant follicle-stimulating hormone (r-FSH; Gonal-F®, Serono, Geneva, Switzerland) and suppression for LH surge was done by a gonadotropin-releasing hormone (GnRH) antagonist, cetrorelix acetate (Cetrotide®, Merck KGaA, Serono, Geneva, Switzerland). Final follicular maturation has been completed by analog trigger; Leuprolide acetate (Lupron; TAP Pharmaceuticals, North Chicago, IL, USA). Lastly, ovum pick-up is performed after 35-36 hours with transvaginal ultrasound. The fertilization process is done with Intracytoplasmic sperm injection (ICSI) for all patients. In our policy, on the fifth day of embryos 1 or 2 good quality embryo transfer (ET) was performed in all ODCs.

2.3. Variables

Variables examined in this study are as follows:

- Recipient's and husband's age,
- The thickness of the endometrium,
- Number of previous ODC attempts
- The number of transferred embryos
- Pregnancy outcomes

2.4. Assessment of pregnancy outcomes

Beta-hCH levels are checked in blood after 12 days, followed by embryo transfer (ET). In case of a positive result, an ultrasound scan is performed after the first beta-hCG test. With an ultrasound scan, foetal viability is checked. International Committee for Monitoring Assisted Reproductive Technology (ICMART) (9) criteria are used for pregnancy results. These are: Biochemical pregnancy has accepted as positive test result which is beta hCG in serum or urine but not seen in ultrasound scan, clinical (ongoing) pregnancy was accepted by the existence of heartbeat of one foetus or more at 7th weeks of gestational age and liveborn of a baby more than 24th weeks was accepted as live birth (LB).

2.5. Statistical analysis

Statistical Package for the Social Sciences v21 (SPSS Inc., Chicago, IL, USA) is used to analyse the data. The normality test is checked by Shapiro-Wilk analyses. Statistical data are shown by mean ± standard deviation or median (interquartile range; IQR). Both parametric and non-parametric tests were used in the situation of the test results. Categorical variables were analysed by the Chi-square tests. Normally distributed variables were analysed with independent samples t-test. The Mann-Whitney U test and Kruskal Wallis test are used for not normally distributed variables. Two-tailed p-values of <0.05 were accepted as statistically significant.

3. Results

The median (IQR) recipient age was 43 (30–54) years. Procedure results revealed that 10.7% was negative, 4.9% was biochemical pregnancy, and 84.4% was clinical pregnancy. Of the clinical pregnancies, miscarriage was observed in 5.7%, preterm delivery in 3.9%, and term delivery in 90.4% of the ODCs. The age of recipients who were younger than 40 years covers 32% of the total participants, for between 40–44 years, 27% and between 45–54 years were 41%. In terms of endometrial thickness (p = 0.059), number of transferred embryos (p = 0.857), number of OD attempt (p = 0.666), live birth rate (p = 0.1, Fig. 1), and other pregnancy outcomes ($p > 0.05$, for all) statistically significant difference was not found out by between age groups (Table 1).

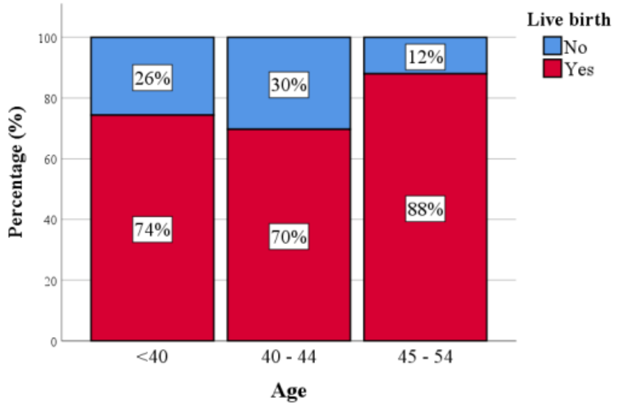

Fig.1. Live birth rates with regard to age groups

Table 1. Summary of clinical characteristics with regard to the age group

	Recipient age (years)				*p-value*
	<40 (n = 39)	40 – 45 (n = 33)	46 – 54 (n = 50)	Total (n = 122)	
Recipient age (years)	34 (30 - 36)	43 (42 - 43)	47 (46 - 50)	43 (37 - 46)	<0.001
Male age (years)	34 (31 - 37)	44 (41 - 49)	46 (41 - 48)	42 (36 - 47)	<0.001
Endometrial thickness (mm)	9.1 (8.7 -11.2)	9.2 (8.4 - 10)	8.7 (8.1 - 9.8)	9.1 (8.3 - 10)	0.059
Embryos transferred (no)					
1	4 (10.3%)	3 (9.1%)	3 (6%)	10 (8.2%)	0.857
2	35 (89.7%)	30 (90.9%)	47 (94%)	112 (91.8%)	
OD attempt (no)					
3	32 (82.1%)	27 (81.8%)	42 (84%)	101 (82.8%)	0.666
2	5 (12.8%)	6 (18.2%)	7 (14%)	18 (14.8%)	
1	2 (5.1%)	0 (0%)	1 (2%)	3 (2.5%)	
Result					
Biochemical pregnancy	3 (7.7%)	2 (6.1%)	1 (2%)	6 (4.9%)	0.439
Clinical pregnancy	31 (79.5%)	27 (81.8%)	45 (90%)	103(84.4%)	0.354
Miscarriage	2 (5.1%)	4 (12.1%)	1 (2%)	7 (5.7%)	0.149
Live birth	29 (74.4%)	23 (69.7%)	44 (88%)	96 (78.7%)	0.100

Data are given as median (1st quartile-3rd quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables, OD: oocyte donation

A total of 96 (78.7%) ODCs resulted in a live birth. In 8.2% (n=10) of cases SET and in 91.8% (n=112) of cases DET were performed. The number of embryos transferred was statistically significantly higher among cases with live births compared to cases without live births (p=0.002). No significant difference was found in; the age of the recipient (p = 0.392), male age (p=0.108), endometrial thickness (p = 0.478), and number of attempts (p=0.777) between cases with and without live birth (Table 2).

Table 2. Summary of characteristics with regard to the live birth

	Live birth		*p-value*
	No (n = 26)	Yes (n = 96)	
Recipient age (year)	42 (44 - 37)	44 (47 - 36)	0.392
Male age (year)	44 ± 6.75	41.45±7.17	0.108
Endometrial thickness (mm)	9.2(10 - 8.6)	9.05 (10.1 - 8.2)	0.478
Embryos transferred (no)			
1	6 (23.1%)	4 (4.2%)	0.002
2	20(76.9%)	92 (95.8%)	
Oocyte donation attempt (no)			
3	22(84.6%)	79(82.3%)	0.777
2	3 (11.5%)	15 (15.6%)	
1	1 (3.8%)	2 (2.1%)	

Data are given as mean ± standard deviation or median (1st quartile-3rd quartile) for continuous variables according to normality of distribution and as frequency (percentage) for categorical variables

4. Discussion

OD had a limited area of use in its first application; however, it has become increasingly common today (1). The decreasing ovarian reserve in women of advanced age may cause infertility. Remarkably, advanced-aged couples who decide to have children pretend to use ODC. This study researched the effects of the number of transferred embryos on expecting live birth rates within fresh ODCs. Recipients' age and other parameters were not affecting the pregnancy outcome. Remarkably, results showed that the live birth rate was higher in women with double embryo transfer compared to single embryo transfer. ODC is generally preferred by relatively advanced-age women. However, advancing age is known to be associated with negative obstetric outcomes in women. Decreased successful pregnancy outcomes in advanced age are suggested to be caused by decreased blood flow to the endometrium, thus limiting the access to various hormones (10). Similarly, different studies showed that the age of recipients over 45 years negatively affects pregnancy outcomes (11-13). Contrary to these studies, many stated that the age of recipients in OD does not affect pregnancy outcomes, which is similar to this study (5, 14-17). Consistent with these studies, no significant difference was found in terms of pregnancy outcomes by the different age groups which are examined in this study. In addition, the husband's age differed between recipient age groups in our results. Previous studies showed that male age in OD does not affect pregnancy outcome (18). Therefore, this difference was assumed not to affect the results. An increased number of embryos transferred in ICSI cycles showed and suggested to increase the probability of implantation and indirectly the possibility of live birth; however, current guidelines recommend SET in OD cycles (3). Multiple pregnancies are not very suitable due to various undesirable consequences and parents' unwillingness. More than one embryo transfer in IVF treatment increases the risk of multiple pregnancies (5, 19). Increased multiple pregnancy frequency with the increasing number of embryo transfers was shown in OD cycles (14, 20). In some studies, no significant difference was shown between DET and SET in terms of pregnancy frequency, but a significant difference was found in terms of multiple pregnancies (21). Among the parameters examined in our study, only the number of transferred embryos was related to the live birth rate. When the number of transferred embryos is compared, DET had significantly higher live birth rates than SET. In different studies, parameters affecting pregnancy outcomes in OD cycles were examined. In a study examining the parameters used to predict egg-sharing donation outcomes, Braga et al. reported that pregnancy outcome was associated with oocyte quality and successful implantation, regardless of the age of donors and recipients (5). In ICSI cycles, the day of the embryo at transfer time is one of the most important reasons referring to the success of blastocyst transfer. Our study shows that DET results have higher LBR compared to SET in ODCs. The reason why DET is recommended may be due to the moderate embryo quality. DET increases fertility per ODC; cumulating single embryo transfer in a fresh or frozen cycle after SET can significantly balance the difference in efficacy while reducing the risks of having multiple pregnancies; at least in women with high-quality embryos (22). On the other hand, concerns about the acceptability of the multiple pregnancy and related complications can be the cost of this decision. In other studies, the authors noted that the recipient's BMI and the husband's sperm quality affect pregnancy outcomes (6, 7, 23). These parameters were not examined in our study. The distribution of these parameters at different levels among the groups may have caused our results to be unconsciously misinterpreted. The most important limitations of this study are retrospective data collected from a single center. Many parameters of the donor, recipients, and husbands that may affect clinical pregnancy in OD treatment were not examined. The fact that these parameters are confounding factors and their heterogeneous distribution among the groups caused us to take a biased interpretation. In addition, age variation of the husband among different recipient age groups may affect the results.

This study exposed that the recipient's age did not significantly affect pregnancy outcomes in ODC. The only parameter affecting the live birth rate in ODC was the number of transferred embryos. Because of this, DET should be preferred to increase live birth rates in ODC cycles if the quality of embryos is not reassuring. Nevertheless, this research only included blastocyst transfer, qualities of the embryos were not included in the study, and the sample size of the population was small. Consequently, it is recommended that the impact of DET and SET with different embryo qualities at blastocyst stages needed to be examined in future studies.

Conflict of interest
The authors declared no conflict of interest.

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