Original Research Article

Comparison of clinical outcomes of "single blastocyst" versus "double blastocyst" transfer in assisted reproductive technology

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Abstract

The transfer of multiple embryos after *in vitro* fertilization (IVF) increases the risk of twins and higher order births. Multiple births are associated with significant health risks and maternal and neonatal complications, as well as physical, emotional, and financial stresses that can strain families and increase the incidence of depression and anxiety disorders in parents. Elective single-embryo transfer (eSET) is among the most effective methods to reduce the risk of multiple births with IVF. Many patients and clinicians have been reluctant to adopt eSET due to studies reporting higher live-birth rates with the transfer of two or more embryos rather than eSET. The aim of the study was to determine whether elective single blastocyst transfer compromises pregnancy outcomes compared to double blastocyst transfer. The study is prospective observational study which included 25 patients with single blastocyst transfer (group 1) and 27 patients with double blastocyst transfer (group 2) as per the inclusion criteria. Controlled ovarian stimulation (COS) with gonadotropin-releasing hormone antagonist protocol was carried out. The treatment outcomes were compared between the two groups. Data described as mean ± standard deviation or percentages. The statistical analysis was performed using Student *t* test, the Chi-squared test, and linear regression models. A *P*-value of <0.05 is considered statistically significant. Statistical analysis was performed with the Statistical Package for Social Sciences (SPSS version 24.0). Statistical analysis showed that the clinical pregnancy rate in the single blastocyst group was 56%, whereas in the double blastocyst group, it was 62.0%. The proportional comparison among the two groups was not found to be statistically significant ($P = 0.319$), but the multiple pregnancy rate was observed to be 70% in double blastocyst group, whereas in single blastocyst group, it was 0%, which was found to be statistically significant ($P = 0.0001$). eSET should be encouraged to decrease incidence of multiple pregnancies and associated complications.

Keywords: Double blastocyst transfer, elective single-embryo transfer, *in vitro* fertilization, multiple pregnancies, single blastocyst transfer

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INTRODUCTION

Increasing success after *in vitro* fertilization (IVF) and intracytoplasmic sperm injection (ICSI) has been accompanied by concerns about rising rates of multiple pregnancies.[1] Multiple pregnancies are associated with increased maternal and perinatal morbidity and mortality, as well as increased costs to the health service.[2,3] Elective single-embryo transfer (eSET) is one of the most important steps of minimizing complications due to multiple pregnancies.

MATERIALS AND METHODS

Inclusion criteria

To participate in the study, women will be required to meet the following inclusion criteria:

(1) Age <35 years
(2) Gonadotropin-releasing hormone (GnRH) antagonist cycles with day 5 blastocyst transfer
(3) Frozen good-quality embryos only (i.e., blastocysts scoring grade 5AA, 5AB, 5BA Gardener's grading system and time-lapse imaging)

Exclusion criteria

(1) Endometrial thickness on day 12 <7 mm
(2) Serum progesterone >1.5 ng/ml on day 2
(3) Ovarian cysts with a diameter >30 mm at day of start of stimulation
(4) Submucosal fibroids
(5) Women with severe comorbidity (insulin-dependent diabetes mellitus, noninsulin-dependent diabetes mellitus, gastrointestinal, cardiovascular, pulmonary, and liver or kidney disease)
(6) Congenital uterine abnormalities
(7) Contraindications or allergies to use of gonadotropins or GnRH antagonists
(8) Severe male factor infertility (oligospermia <1 million/ml, and azoospermia)

A prospective, observational study conducted between October 2020 and March 2021, in a private IVF center (Wings IVF Centre, Ahmedabad). A total of 52 patients, which included 25 patients with single blastocyst transfer (group 1) and 27 patients with double blastocyst transfer (group 2), undergoing IVF during the period of the study were screened to determine whether they fulfilled the inclusion criteria [Table 1]. Ovarian stimulation with GnRH antagonist protocol was used in both the groups. Stimulation was performed using combination of injection recombinant follicle stimulation hormone (rFSH) (Gonal F, Merck, Folligraf, Bharat Serums), and injection human menopausal gonadotropin (HMG) (Gynogen, Bharat Serums), maintaining the physiological synergy of FSH and luteinizing hormone (LH) ratio of 2:1, which was started on day 2 or 3 of menses. Follicular monitoring, human chorionic gonadotropin (hCG) trigger, and ovum pick up were carried out as per protocol. After 3 to 4 hours of ovum pick up, ICSI was performed and further embryo growth was monitored with time lapse technique.

Grading of embryo was performed with "Gardner" blastocyst grading system. All the embryos were vitrified at blastocyst stage for later on transfer, one group chosen for single blastocyst and other for double blastocyst transfer after 1 month after proper consent. Transfer of embryos was performed only when progesterone levels were ≤1.5 ng/ml on day 2 and the endometrium was 7 mm or more on 12th day of estradiol valerate. After embryo transfer, luteal-phase support was given as per protocol. Primary outcome was measured in the form of clinical pregnancy defined as confirmation of pregnancy by both, high level of serum beta-hCG and presence of gestational sac along with cardiac activity of fetus 30 days after the embryo transfer, observed by ultrasonogram. Ongoing pregnancy was the secondary outcome, defined as viable intrauterine pregnancy of at least 12 weeks duration confirmed on an ultrasonography scan.

RESULTS

Statistical analysis was performed with the Statistical Package for Social Sciences (SPSS version 24.0, IBM

Table 1: Age-wise distribution of women in both the groups

Age group	Single-embryo transfer		Double-embryo transfer	
	N	%	*N*	%
21–25	4	16	2	7.407407
26–30	11	44	16	59.25926
31–35	10	40	9	33.33333
Total	25	100	27	100
Mean age (±SD), years	29.36 ± 3.19		29.48 ± 3.01	
t value	0.13 df = 50			
P-value	0.88			

df, degrees of freedom; SD, standard deviation.

Company). Statistical software was used for calculating the *P*-values. Comparison of mean between the two groups was carried out using unpaired *t* test and comparison of proportions between the two groups was performed using *Z* test for two sample proportion. A *P*-value of <0.05 was considered as statistically significant.

The final data were presented in the form of tables and graphs. Statistical analysis showed that the clinical pregnancy rate in the single blastocyst group was 56%, whereas in the double blastocyst group, it was 62.0% [Table 2]. The proportional comparison among the two groups was not found to be statistically significant ($P = 0.319$), but the multiple pregnancy rate was observed to be 70% in double blastocyst group, whereas in single blastocyst group, it was 0%, which was found to be statistically significant ($P = 0.0001$) [Table 3].

DISCUSSION

The present study confirms the notion that in infertile patients less than 35 years with potential, favorable outcome, single blastocyst transfer can achieve comparable implantation rate, clinical pregnancy rate, and ongoing pregnancy rate as that of double blastocyst transfer, meanwhile decreasing the chances of multiple pregnancy rates.

In our study, clinical pregnancy rate was 56% in eSET, whereas 62% in double embryo transfer (DET). Abuzeid *et al.*[4] conducted randomized controlled trial (RCT) "The impact of single versus double blastocyst transfer on pregnancy outcomes" which included 50 patients with single blastocyst transfer (group 1) and 50 patients with double blastocyst transfer (group 2) found lower clinical pregnancy rates in group 1 (61.2% vs. 80.0%) but significantly higher multiple pregnancy rates in group 2 (35.0%) compared to group 1 (0%).

Pandian *et al.*[5] included 14 randomized controlled trials found no difference in cumulative live-birth rate when single cycle of DET compared with separated SET (45% chance of live birth following a single cycle of DET and with SET, it would be between 24% and 33%) but multiple pregnancy rates differ (14% in DET and with SET would be between 1% and 3%).

The same thing is supported by Kamath *et al.*[6] which included 17 RCTs ("Number of embryos for transfer following IVF or ICSI") concluded that there is 15% risk of multiple pregnancy following single cycle of DET, with SET, it would be 2%.

In our study, eSET also demonstrated its safety because this strategy reduced multiple pregnancy rates 0% in eSET versus 70% in DET. Similarly, the analysis of data from 2004 to 2013 of the ASRM study (2017), which conducted both fresh and frozen-embryo transfer cycles in young patients (<35 years old), showed that clinical pregnancy rate in the eSET D3 decreased by 15% compared to that of DET D3, whereas eSET D5 decreased by 10% compared to DET D5. With eSET D5, multiple pregnancy rate decreased 22% to 47% compared to DET D5; with eSET D3, this rate decreased by 22% to 28% compared to DET D3 in patients under 38 years old.[7]

Retrospective study was reported by Racca included 3601 women who underwent first frozen-embryo transfer showed that ongoing pregnancy rates between the

Table 2: Comparison of clinical pregnancy rates in the two groups

Parameter	Single-embryo transfer		Double-embryo transfer
Total number of women	25		27
Positive	14		17
Negative	10		10
Pregnancy rate	56%		62%
Z test (single vs. double)		$Z = 0.47$	
P-value		0.319*	

Table 3: Comparison of multiple pregnancy rates in the two groups

Parameter	Single-embryo transfer		Double-embryo transfer
Total number of women	14		17
Positive	0		12
Negative	0		5
Pregnancy rate	0%		70%
Z test (single vs. double)		$Z = 4.3$	
P-value		0.0001*	

SET and DET were similar following blastocyst-stage embryo transfer (18.5% vs. 18.9%, respectively), whereas multiple delivery rates were significantly higher in women with DET compared to SET (16.7% vs. 1.9%; $P < 0.001$).[8-10]

According to another study of Freeman[11] cohort study of 678 FET cycles, live-birth rate between eSET D5 and DET D5 were similar (54–62% vs. 54–66%, $P = 0.696$) and multiple pregnancy rate decreased significantly with eSET D5 compared to DET D5 (0–3% vs. 24–65%, $P < 0.05$) in good prognosis patients (under 38 years of age at oocyte collection, having at least two frozen blastocysts, and undergoing their first autologous FET cycle).

The results of our study demonstrate that eSET D5 strategy in combination with selected embryos transferred by time-lapse imaging in good prognosis patients is the best strategy.

CONCLUSION

The eSET in good prognosis patients should be a choice to minimize the risk of multiple pregnancies, while achieving acceptable live birth and neonatal outcomes. The strategy of elective single blastocyst transfer for good prognosis patients was an optimal option that ensured a balance between live-birth outcomes and minimizing the risk of multiple pregnancies.

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Conflicts of interest
There are no conflicts of interest.

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