Impact of Transferring a Poor Quality Embryo Along with a Good Quality Embryo on Pregnancy Outcomes in IVF/ICSI Cycles: a Retrospective Study

Auswirkungen des Transfers eines Embryos von schlechter Qualität zusammen mit einem Embryo von guter Qualität auf das Schwangerschafts-Outcome: eine retrospektive Studie

OPEN ACCESS

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Key words

double embryo transfer, embryo quality, cleavage stage, blastocyst stage, live birth rate, multiple pregnancy

Schlüsselwörter

Doppelembryonentransfer, Embryoqualität, Teilungsstadium, Blastozystenstadium, Lebendgeburtenrate, Mehrlingsschwangerschaft

received	28.3.2020
accepted after revision	7.7.2020

Bibliography

DOI https://doi.org/10.1055/a-1213-9164

Geburtsh Frauenheilk 2020; 80: 844–850 © Georg Thieme Verlag KG Stuttgart · New York | ISSN 0016-5751

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ABSTRACT

Background The number and the quality of embryos transferred are important predictors of success in in vitro fertilization (IVF) cycles. In the presence of more than one good quality embryo on the transfer day, double-embryo transfer (DET) can be performed with these embryos, but generally, different quality embryos are present in the available transfer cohort. We aimed to investigate the effect of transferring a poor quality embryo along with a good quality embryo on IVF outcomes.

Methods In this study, 2298 fresh IVF/intracytoplasmic sperm injection (ICSI) cycles with two good quality embryos (group A), one good and one poor quality embryo (group B), and single good quality embryo (group C) transfers were examined. All groups were divided into two subgroups according to the transfer day as cleavage or blastocyst stage. Clinical pregnancy and live birth rates were the primary outcomes.

Results In the cleavage stage transfer subgroups, the clinical pregnancy rates were lower in the single-embryo transfer (SET) subgroup compared with DET subgroups, but the difference was not statistically significant compared with DET with mixed quality embryos. The live birth rates were comparable between the three groups. In the blastocyst transfer subgroups, the clinical pregnancy and live birth rates were significantly higher in DET with two good quality embryos than DET with mixed quality embryos and SET groups. Multiple pregnancy rates were higher in both DET groups in terms of transfer day ($p = 0.001$).

Conclusion DET with mixed quality embryos results with lower clinical pregnancy and live birth rates compared with DET with two good quality embryos at the blastocyst stage. At cleavage stage transfer, there is no difference in live birth rates between the two groups.

ZUSAMMENFASSUNG

Hintergrund Anzahl und Qualität von transferierten Embryos sind wichtige Prädiktoren für den Erfolg bei In-vitro-Fertilisations-(IVF-)Zyklen. Wenn mehr als ein Embryo von guter Qualität am Transfertag vorhanden ist, kann ein Doppelembryonentransfer (DET) mit diesen Embyros vorgenommen werden. Generell sind aber die verfügbaren Embryos von sehr

unterschiedlicher Qualität. Ziel dieser Studie war es, die Auswirkung eines Transfers von einem Embryo schlechter Qualität zusammen mit einem Embryo guter Qualität auf das IVF-Outcome zu untersuchen.

Methoden In dieser Studie wurden 2298 frische IVF/intrazytoplasmatische Spermieninjektions-(ICSI-)Zyklen, bei denen entweder 2 Embryos von guter Qualität (Gruppe A), ein Embryo von guter Qualität und ein Embryo von schlechter Qualität (Gruppe B), oder ein einziges Embryo von guter Qualität (Gruppe C) transferiert wurden, verglichen. Alle diese Gruppen wurden je nach Transfertag (im Teilungsstadium bzw. Blastozystenstadium) nochmals in 2 Untergruppen unterteilt. Die primären Endpunkte waren klinische Schwangerschaftsrate und Lebendgeburtenrate.

Ergebnisse In den Teilungsstadiumtransfer-Untergruppen waren die klinischen Schwangerschaftsraten niedriger in der Untergruppe mit einem einzigen transferierten Embryo (SET) verglichen mit den DET-Untergruppen, aber der Unterschied zu den DET-Untergruppen mit Embyros gemischter Qualität war nicht statistisch signifikant. Die Lebendgeburtenraten waren bei allen 3 Gruppen vergleichbar. Bei den Blastozystentransfer-Untergruppen waren die klinischen Schwangerschaftsraten und Lebendgeburtenraten signifikant höher in der DET-Untergruppe mit 2 Embyros guter Qualität verglichen mit der DET-Untergruppe mit Embryos gemischer Qualität und den SET-Untergruppen. Die Mehrlingsschwangerschaftsraten waren in beiden DET-Gruppen höher ($p = 0{,}001$).

Schlussfolgerung DET mit Embryos von gemischter Qualität geht einher mit niedrigeren klinischen Schwangerschaftsraten und Lebendgeburtenraten als DET mit 2 Embryos von guter Qualität im Blastozystenstadium. Werden die Embryos im Teilungsstadium transferiert, gibt es hinsichtlich der Lebendgeburtenraten keinen Unterschied zwischen den 2 Gruppen.

Introduction

The number and quality of embryos transferred are important in determining the success of assisted reproductive technology (ART) treatment cycles. Good quality embryo transfers result in higher clinical pregnancy and live birth rates [1], and poor quality embryo transfers result in higher miscarriage and lower ongoing pregnancy rates [2]. This is probably the result of different endometrial responses to the quality of the embryo; decidualized endometrial stromal cells have been shown to act as biomarkers for arrested embryos, thus preventing implantation [3]. Clinical pregnancy and live birth rates are lower with single poor quality embryo transfers; however, when clinical pregnancy is achieved, miscarriage rates, obstetric, and perinatal outcomes are similar to good quality embryo transfer cycles [1]. Therefore, a poor quality embryo may also have the chance of a live birth.

There is increasing preference for elective single-embryo transfers (SET) in in vitro fertilization (IVF) cycles because cumulative live birth rates are high after fresh cycles followed by frozen and thawed cycles with SET [4]. However, double-embryo transfers (DET) are still preferred in many IVF clinics because the clinical pregnancy and live birth rates are higher than with SET cycles [5, 6]. Nevertheless, it is also known that multiple pregnancy rates are higher in DET, resulting in higher maternal and perinatal mortality and morbidity rates [5,6]. When there is more than one good quality embryo on the transfer day, many clinics prefer DET, but generally, there are embryos of different qualities in the available transfer cohort. It is difficult to decide whether to transfer the mixed quality embryos together or to transfer a single good quality embryo, because a good quality embryo has been shown to have a higher implantation rate than DET with mixed quality embryos [7].

The aim of this study was to investigate whether a poor quality embryo transfer along with a good quality embryo had a negative effect on IVF outcomes compared with DET with two good quality embryos.

Materials and Methods

Study design

The presented retrospective clinical study was conducted at the ART clinic of Health Sciences University Etlik Zubeyde Hanım Women's Health Teaching and Research Hospital, Ankara, Turkey. The patient files between January 2007 and February 2018 were reviewed using a computer-based database. The IVF cycle was accepted as the process that started with controlled ovarian stimulation (COH) and resulted with embryo transfer. We analyzed 2298 fresh cycles of women aged ≤ 40 years who had their first, second or third cycles with SET or DET. The patients were divided into three groups: group A included two good quality embryo transfer cycles, group B included one good and one poor quality embryo transfer cycle, and group C included a single good quality embryo tranfer cycle. All groups were divided into two subgroups according to the stage of the embryo transferred as cleavage stage (day 3) or blastocyst (day 5) transfer subgroups. Patients with endometrial, uterine pathologies, endometriosis or hydrosalpinx were excluded. The study was approved by the institutional ethics committee (12/11/2018–19). Formal consent was not required because it was a retrospective study.

Ovarian stimulation, intracytoplasmic sperm injection (ICSI), and embryo transfer procedures

Patients were stimulated with standard-antagonist or long-agonist protocols after evaluation of the ovarian reserve. The dose of gonadotropins was individualized according to the patient's age, basal serum follicle-stimulating hormone (FSH) level, antral follicle count (AFC), and body mass index (BMI), and was adjusted depending on the ovarian response. Cycle monitorization with serial transvaginal ultrasonography and measurement of serum estradiol (E2), luteinizing hormone (LH), and progesterone levels were continued until human chorionic gonadotropin (hCG) administration for final oocyte maturation when at least three follicles reached a mean diameter of 18 mm. Oocyte pick-up (OPU) was

performed using transvaginal ultrasound-guided aspiration 35.5–36 hours after the hCG administration.

The mature oocytes were inseminated by using ICSI. Embryo transfer was performed under transabdominal ultrasonographic guidance. All patients received luteal phase support (Crinone 8% gel, Serano, Istanbul) starting on the day of oocyte retrieval until a pregnancy test was performed. Serum hCG levels were measured 14 days after OPU. Positive values (hCG > 10 IU/L) were repeated after 2–4 days, and in cases of pregnancy, luteal phase support was continued up to 10–12 weeks of gestation.

Assesment of embryo development

The fertilization of the oocytes was assessed 18–20 hours after ICSI with the observation of the presence of two pronuclei. Day 2 embryos (42–44 h after ICSI) were classified according to the size, nucleation, and cytoplasmic morphology of the blastomers. Day 3 embryos (61–65 h after ICSI) were graded using an embryo scoring system according to the number, size, and symmetry of the cells and degree of fragmentation [8] (▶ **Table 1**). Grade 1 and grade 2 embryos were classified as good quality embryos, grade 3 and grade 4 embryos were classified as poor quality embryos for cleavage stage embryos. Grade 5 embryos were not transferred. Blastocyst-stage embryo scoring was based on the number and adhesion of evenly sized blastomers, visible inner cell mass, and blastocyst cavity, continuous trophoectoderm with sufficient cells, and zona pellucida thickness, as proposed by Gardner et al. [9] (▶ **Table 2**). Blastocysts with ≥ 3 BB score were classified as good quality embryos.

Clinical outcome

The determination of an embryo with a positive heart beat in a transvaginal scan (TVS) was defined as a clinical pregnancy. The clinical pregnancy rate was defined as the number of heart beat-positive embryo detected through ultrasonography divided by the number of embryo transfers. Live birth was defined as delivery of a viable infant after 22 weeks of gestation. The live birth rate was defined as the number of live offspring delivered divided by the number of embryo transfers. The miscarriage rate was defined as the percentage of pregnancy losses before 20 weeks of gestation among all clinical pregnancies. The obstetric outcomes of the pregnancies in all three groups were also recorded and compared.

▶ **Table 1** Embryo grading according to the cleavage stage embryo scoring system [8].

Score	Description
Grade 1	Embryo with 8–12 even sized blastomeres and < 5% cytoplasmic fragments
Grade 2	Embryo with 6–10 even sized blastomeres, 5–20% cytoplasmic fragments
Grade 3	Embryo with uneven blastomeres, ≤ 20% cytoplasmic fragments
Grade 4	Embryo with even or uneven sized blastomeres, 20–50% cytoplasmic fragmentation
Grade 5	Embryo with ≤ 4 blastomeres of any size, > 50% or complete fragmentation

Grade 1 and grade 2 embryos were classified as good quality embryos, grade 3 and grade 4 embryos were classified as poor quality embryos; grade 5 embryos were not transferred.

Statistical analysis

A power analysis was conducted using the G*Power (version 3.1.7) software and based on findings of comparable studies [7, 10]. An effect size of 0.237 was used with power set at 0.85 and α at 0.05 to determine that a sample size of 163 was required in each group to conduct one-way analysis of variance (ANOVA). Statistical analyses were completed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) version 20.0 software. The variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogrov-Simirnov/Shapiro-Wilk test) to determine whether they were normally distributed. ANOVA was used to compare continuous variables with normal distributions and the Kruskal-Wallis test was used to com-

▶ **Table 2** Embryo grading according to the blastocyst stage embryo scoring system [9].

Expansion grade	Description		
1	Blastocoel cavity less than half of the embryo volume		
2	Blastocoel cavity more than half of the embryo volume		
3	Full blastocyst, cavity completely filling the embryo		
4	Expanded blastocyst, cavity larger than the embryo, with thinning of the shell		
5	Hatching out of the shell		
6	Hatched out of the shell		
Grade	**A**	**B**	**C**
Inner cell mass	Many cells, tightly packed	Several cells, loosely grouped	Very few cells
Trophoectoderm	Many cells, forming a cohesive layer	Few cells, forming a loose epithelium	Very few large cells

Blastocysts with ≥ 3 BB (AA, AB, BA, BB) score were classified as good quality embryos. Blastocysts graded as AC, CA, BC, CB and CC were classified as poor quality embryos.

▶ **Table 3** Comparison of IVF-ET treatment cycle characteristics of the patients in group A, group B and group C.

	Group A (DET with GQE's) n = 498	Group B (DET with MQE) n = 179	Group C (SET with GQE) n = 1621	p*
Maternal age, years	33.5 ± 4.6	34.5 ± 4.3	29.2 ± 4.3	**0.001**[b,c]
Body mass index, kg/m^2	26.6 ± 5.0	26.6 ± 4.5	26.0 ± 4.9	0.054
Total gonadotropin dose, IU	2557.1 ± 1042.3	2898.0 ± 1172.7	2249.3 ± 957.9	**0.001**[d]
Number of mature oocytes	9.3 ± 5.4	7.1 ± 4.0	8.9 ± 5.7	**0.001**[a,c]
Number of fertilized oocytes	5.3 ± 3.5	3.6 ± 2.3	4.8 ± 3.6	**0.001**[d]
Fertilization rate	0.60 ± 0.22	0.55 ± 0.26	0.56 ± 0.25	**0.002**[d]
Endometrial thickness, mm	10.1 ± 2.3	10.5 ± 5.6	10.3 ± 2.3	0.178

Data presented as mean ± SD. DET: double embryo transfer; GQE: good quality embryo; MQE: mixed quality (one good quality plus one poor quality) embryos; SET: single embryo transfer.

[a] There was a significant difference between DET with GQE and DET with MQE.

[b] There was a significant difference between DET with GQE and SET with GQE.

[c] There was a significant difference between DET with MQE and SET with GQE.

[d] There was a significant difference between DET with GQE, DET with MQE and SET with GQE.

* p-values with statistical significance ($p < 0.05$) are shown in bold.

pare variables with non-normal distributions. The χ^2 test was used to compare the proportions in different groups. A p value < 0.05 was accepted as statistically significant.

Results

Patient and tratment characteristics

Out of the 2298 cycles analyzed, 498 patients were in group A (DET with two good quality embryos), 179 in group B (DET with one good and one poor quality embryo), and 1621 in group C (SET with a good quality embryo). The demographic and cycle characteristics of the three groups are shown in ▶ **Table 3**. The patients in group C were statistically significantly younger than in the other two groups (p = 0.001) because the legislation related to ART procedures in our country prohibits DET in the first and second cycles before age 35 years, but DET is allowed either in the third cycle and beyond independent of age or in all cycles in women aged over 35 years. The total gonadotropin dose used for ovarian hyperstimulation was significantly higher, and the number of mature and fertilized oocytes was significantly lower in group B when compared with the other two groups.

IVF and pregnancy outcomes by embryo stage at transfer: cleavage embryo transfer

The groups were divided into subgroups according to the stage of the embryo transferred. In cleavage stage (D3) transfer subgroups, there were 324 patients in group A, 127 patients in group B, and 887 patients in group C. When cleavage stage embryo transfers were analyzed, the clinical pregnancy rates of group A and group B were similar (39.2 vs. 38.1%), and group C had the lowest clinical pregnancy rates (30.7%), which was statistically significantly lower than in group A (p = 0.011). Live birth rates were similar in all groups. The miscarriage rate was lowest in group C (15.2%) compared with groups A (24%) and B (25%), but the difference was not statistically significant (p = 0.057). Multiple pregnancy and preterm delivery rates were statistically significantly higher in group A and group B (▶ **Table 4**).

IVF and pregnancy outcomes by embryo stage at transfer: blastocyst embryo transfer

In the blastocyst transfer subgroups, there were 174 patients in group A, 52 in group B, and 734 in group C. In these subgroups, the clinical pregnancy rates were significantly higher in group A than in groups B and C (57.5, 27.5, 42.6%, respectively; p = 0.001). The live birth rate was significantly higher in group A than in group B (40.2 vs. 19.2%, p = 0.011). The clinical pregnancy and live birth rates were higher in group C than in group B, but it was not statistically significant. There was no statistically significant difference in miscarriage rates. Multiple pregnancy rates were significantly higher in patients in group A and group B (▶ **Table 5**).

IVF and pregnancy outcomes of DET with mixed quality embryos in both stages

For patients in group B, in cleavage stage transfers, clinical pregnancy (38.1%) and live birth (26.0%) rates were higher than in blastocyst stage transfers (27.5 and 19.2%, respectively), but the difference was not statistically significant (p = 0.179 and p = 0.287). The miscarriage rate was similar in both embryo transfer stages. However, the multiple pregnancy rate was higher in blastocyst stage transfers (28.6%) than in cleavage stage transfers (13.0%), although it did not reach statistical significance (p = 0.172).

▶ **Table 4** Comparison of the reproductive outcomes of IVF cycles with cleavage stage embryo transfer in group A, group B and group C.

	Group A (DET with GQE's) n = 324	Group B (DET with MQE) n = 127	Group C (SET with GQE) n = 887	p*
Clinical pregnancy rate	125 (39.2)	48 (38.1)	271 (30.7)	**0.011**[b]
Live birth rate	89 (27.5)	34 (26.8)	217 (24.5)	0.593
Miscarriage rate	30 (24)	12 (25)	40 (15.2)	0.057
Multiple pregnancy rate	28 (22.8)	6 (13)	8 (3.4)	**0.001**[b,c]
Preterm delivery	15 (12.0)	4 (8.3)	7 (2.6)	**0.001**[b,c]

Data presented as mean ± SD. DET: double embryo transfer; GQE: good quality embryo; MQE: mixed quality (one good quality plus one poor quality) embryos; SET: single embryo transfer.

[a] There was a significant difference between DET with GQE and DET with MQE.

[b] There was a significant difference between DET with GQE and SET with GQE.

[c] There was a significant difference between DET with MQE and SET with GQE.

[d] There was a significant difference between DET with GQE, DET with MQE and SET with GQE.

* p-values with statistical significance ($p < 0.05$) are shown in bold.

▶ **Table 5** Comparison of the reproductive outcomes of IVF cycles with blastocyst embryo transfer in group A, group B and group C.

	Group A (DET with GQE's) n = 174	Group B (DET with MQE) n = 52	Group C (SET with GQE) n = 734	p*
Clinical pregnancy rate	100 (57.5)	14 (27.5)	309 (42.6)	**0.001**[a,b]
Live birth rate	70 (40.2)	10 (19.2)	234 (31.9)	**0.011**[a]
Miscarriage rate	23 (23.0)	3 (21.4)	58 (18.8)	0.609
Multiple pregnancy rate	32 (32.7)	4 (28.6)	8 (2.6)	**0.001**[b,c]
Preterm delivery	7 (7.0)	1 (7.1)	11 (3.6)	0.313

Data presented as mean ± SD. DET: double embryo transfer; GQE: good quality embryo; MQE: mixed quality (one good quality plus one poor quality) embryos; SET: single embryo transfer.

[a] There was a significant difference between DET with GQE and DET with MQE.

[b] There was a significant difference between DET with GQE and SET with GQE.

[c] There was a significant difference between DET with MQE and SET with GQE.

[d] There was a significant difference between DET with GQE, DET with MQE and SET with GQE.

* p-values with statistical significance ($p < 0.05$) are shown in bold.

Discussion

Despite new advances in the field of ART, factors that influence implantation are still unclear. In this study, we aimed to evaluate the effect of a poor quality embryo transfer along with a good quality embryo on IVF outcomes. Our study was different from previous studies because we compared the pregnancy outcomes according to the stage of the transferred embryos, cleavage stage and blastocyst stage.

The number and the quality of transferred embryos are important predictors of IVF cycle outcomes. Good quality embryo transfers result in higher clinical pregnancy and live birth rates [1, 11]. Although ongoing pregnancy rates have been shown to be lower [2], poor quality embryos may also have the chance of clinical pregnancy, and when clinical pregnancy is achieved, live birth rates and pregnancy outcomes can be similar with good quality embryo transfer pregnancies [1]. In our study group, when one good and one poor quality embryo was transferred, the live birth rates were statistically significantly lower than two good quality embryo transfers on blastocyst stage transfers, but were not different on cleavage stage transfers. The live birth rates with SET with a good quality embryo were similar to DET with two good quality embryos in both transfer stages, but higher than DET with mixed quality embryos in the blastocyst transfer subgroup. The pregnancy complications apart from preterm delivery were similar in all three groups.

In IVF treatment cycles, DET is performed in many clinics because clinical pregnancy rates are higher than with SET. In a fresh IVF cycle after DET, the live birth rate is reported as 40 %, whereas it ranges between 22 and 30 % after SET [12]. However, cumulative live birth rates are high after fresh cycles followed by frozen and thawed cycles with SET in a remarkable number of countries practicing elective SET [4]. On the other hand, multiple pregnancy rates are significantly high in patients receiving DET cycles. When

there are two good quality embryos available for transfer, DET is performed although the multiple pregnancy risk is taken into account. Whether DET with a good quality embryo accompanied by a poor quality embryo demonstrates similar results is debatable. It is known that morphologically poor quality embryos are more likely to be genetically abnormal, and theoretically, a poor quality embryo may impair the implantation of the good quality embryo when transferred together. The question is whether the poor quality embryo impairs the implantation potential of the good embryo when transferred together or each transferred embryo has its own implantation potential.

A series of studies reported that group culture of embryos had a beneficial effect on embryo development and growth [13 – 15]. There is growing evidence of an interaction among embryos that is mediated by specific released growth factors, which promote their own development. In contrast, it has also been demonstrated that this interaction depends highly on the quality of cultured embryos [16]. The presence of poor quality embryos in the embryo culture may result in a lower blastulation rate of all embryos in comparison with good quality embryos cultured together. In Tao et al.'s study, poor quality embryos reduced blastocyst development when cultured with good quality embryos [16], suggesting a negative effect on implantation, but there was no effect on clinical pregnancy and live birth rates. Besides, there are studies proving that the endometrium acts as a biosensor [17], and prevents abnormal embryos from implanting [3].

El-Danasouri et al. concluded that morphologically and developmentally impaired embryos significantly reduced the implantation chance of good quality embryos, independent of the transfer date [18]. By contrast, Li et al. and Wintner et al. reported that the poor quality embryos did not impair the implantation of good quality embryos when transferred together [7, 19].

Blastocyt stage transfers are widely preferred in order to increase the reproductive outcome of ART cycles because a vast number of studies have shown that the predictive value of morphological assessment of day 3 embryos for embryonic development is limited and the risk of aneuploidy is significantly lower in day 5 embryos [20 – 22]. Therefore, as much as embryo quality, transfer stage can also be important in determining treatment cycle success.

Dobson et al. reported that DET of mixed quality embryos at the blastocyst stage did not increase the live birth rate when compared with SET with a good quality embryo [10], it was even possible that a poor quality embryo might have a detrimental impact on blastocysts used during DET.

In our study, we found that in patients undergoing blastocyst transfer, the live birth rates in DET with mixed quality embryos were lower than with DET with two good quality embryos. The live birth rates in the SET group with a good quality embryo were higher than in the DET group with mixed quality embryos, but the differences between the groups did not reach statistical significance.

Li et al. found that in patients undergoing cleavage stage embryo transfer, there was no difference between DET with two good quality embryos and DET with a poor quality embryo and a good quality embryo in terms of clinical pregnancy and live birth rates [19]. Similarly, we found that patients undergoing cleavage stage embryo transfer had similar clinical pregnancy rates to the DET group with two good quality embryos, and DET with one good and one poor quality embryo. SET with a good quality embryo resulted in significantly lower clinical pregnancy rates, but the live birth rates were comparable between the three groups ($p = 0.59$).

Previous studies showed that multiple pregnancy rates were increased with DET [5, 6, 23, 24]. Interestingly, Li et al. reported a higher multiple pregnancy rate in DET with two good quality embryos when compared with DET with one good and one poor quality embryo, and related this finding with the higher implantation rate of good quality embryos. In our study, the multiple pregnancy rate was higher in both DET groups compared with the SET group.

Previous studies have shown that clinical pregnancy achieved with a poor quality embryo had a similar chance of reaching live birth as a high quality embryo pregnancy [1, 6]. Consistent with other studies, we found no statistically significant differences in terms of miscarriage and ectopic pregnancy rates between the groups [6, 7, 19]. The miscarriage rate was almost significantly lower in the cleavage stage SET group, which was probably due to the younger age of this group; the incidence of aneuploidy is expected to be lower in this group.

In contrast to Gelbaya et al.'s study [25], we found that preterm delivery rates were significantly high in DET subgroups in accordance with the increased multiple pregnancy rates. In the cleavage stage transfer subgroups, preterm delivery rates were significantly high in DET subgroups ($p = 0.01$); however, the difference was not statistically significant for the blastocyst transfer subgroups ($p = 0.31$).

The main limitation of our study is the retrospective case-control design and the younger age of the SET group patients due to legislation related to ART procedures in our country. The low patient number in group B at the blastocyst stage may be a limiting factor. Another universal limitation is the subjective morphologic assessment of the embryo, even when performed by experienced embryologists. More advanced methods to evaluate embryos will provide a better definition of good and poor quality embryos.

In conclusion, DET with mixed quality embryos has lower clinical pregnancy rates and live birth rates compared with DET with two good quality embryos at the blastocyst stage, but there is no difference between DET groups with cleavage stage transfer. Transferring a poor quality embryo with a good quality embryo does not influence miscarriage and multiple pregnancy rates in both cleavage and blastocyst stage transfers.

Author Contributions

Conception and design: OA, RO, SD; Project development: IK, OMT; Data analysis: EB, BD; Writing the Manuscript: OA, RO.

Conflict of Interest

The authors declare that they have no conflict of interest.

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