



Evaluation of Fertility Success Rate with Simultaneous Transfer of Embryos with Different Qualities in IVF/ICSI Candidates

Sima Janati¹, Mohammad Amin Behmanesh², Sarah Madani³ and Seyedeh Mahsa Poormoosavi^{4,*}

¹Department of Obstetrics and Gynecology, Research and Clinical Center for Infertility, School of Medicine, Dezful University of Medical Sciences, Dezful, Iran

²Department of Histology, School of Medicine, Dezful University of Medical Sciences, Dezful, Iran

³School of Medicine, Dezful University of Medical Sciences, Dezful, Iran

⁴Department of Histology, Research and Clinical Center for Infertility, School of Medicine, Dezful University of Medical Sciences, Dezful, Iran

*Corresponding author: Department of Histology, Research and Clinical Center for Infertility, School of Medicine, Dezful University of Medical Sciences, Dezful, Iran. Email: m.poormoosavi@gmail.com

Received 2022 May 20; Revised 2022 December 06; Accepted 2022 December 07.

Abstract

Background: One of the most important factors in the success of assisted reproductive techniques is the quality of the embryo generated in the laboratory. Whether to transfer only one high-quality embryo or a combination of high- and low-quality embryos is a dilemma.

Objectives: The present study reviewed the embryo transfer records of IVF/intra cytoplasmic sperm injection (ICSI) patients in Dezful Infertility Center, Iran, to evaluate the impact of the simultaneous transfer of a low-quality embryo on the growth and implantation of a high-quality embryo and live birth.

Methods: This cross-sectional study evaluated the files and records of 802 patients undergoing IVF/ICSI at Dezful Infertility Treatment Center from 2013 to September 2020. The patients were classified into group 1: Patients with the transfer of only one grade A (equal blastomeres without fragmentation) embryo, group 2: Patients with the transfer of two grade A and B (equal blastomeres with slight fragmentation) embryos, group 3: Patients with the transfer of two grade A and C (unequal blastomeres with or without fragmentation) embryos, and group 4: Patients with the transfer of two grade C and B embryos.

Results: The mean age of women and men was 32.52 ± 5.10 and 37.59 ± 6.60 years, respectively. Age, duration of infertility, cause of infertility, endometrial diameter, estradiol level, oocyte number, and embryo number had no significant differences between the groups ($P > 0.05$). Also, the findings indicated no significant differences between the groups in terms of implantation rate, live birth rate, fertility rate, multiple pregnancies rate, and chemical and clinical abortions ($P > 0.05$).

Conclusions: It seems that the simultaneous transfer of embryos with different qualities does not affect the success rate and fertility outcomes in IVF/ICSI candidates.

Keywords: Infertility, Embryo Transfer, Embryo Quality, Fertility Outcome

1. Background

Fertility, or the ability to have a child, is considered an accomplishment in reproduction and the beginning of new life for couples. On the other hand, infertility, by disrupting reproduction, has always had many unintended consequences for couples, sometimes treatable and sometimes incurable (1). It is estimated that 9% of couples all around the world have experienced some form of infertility, and 56% of them seek medical care for infertility (2). One of the most important factors in the success of assisted reproductive techniques (ART) is the quality of the embryo generated in the laboratory (3).

Many studies have demonstrated the close association of fetal morphology and quality with implantation rate

and clinical fertility; however, a low-quality embryo also has the potential to provide fertility. On the other hand, low-quality embryos may further increase spontaneous abortions and reduce the total rate of pregnancy (4). Some studies indicate that the rate of clinical pregnancy and live birth in high-quality embryo transfer is twice the clinical pregnancy with a poor-quality one. However, there has been a similar chance of conceiving a clinical pregnancy that terminates in a live birth with low- and high-quality embryos (5). Some researchers also believe that in women under 36, the cumulative live birth rate can vary from 40% to 64%, depending on the quality of the fetus (6).

In addition, it has been shown that the simultaneous transfer of two embryos, compared with one embryo, increases the chances for fertility and live birth. Hence, the

chance is one-third when one embryo is transferred compared with when two embryos are transferred (7). This is why most embryologists in infertility treatment centers around the world try to increase the number of transferred embryos when the quality of the embryos is low in the cleavage stage. Despite that, the decision to transfer only one high-quality embryo or two high- and low-quality embryos simultaneously is tough, and the question arises whether the simultaneous transfer of a low-quality embryo can reduce the implantation chance of the high-quality one. Some researchers believe that there is a paracrine interaction between embryos before implantation, which can affect the growth of concomitant and juxtaposed embryos (8). Studies have also shown that the simultaneous presence of a low-quality embryo in a culture medium reduces the growth rate and blastulation of other embryos (9).

2. Objectives

the purpose of this retrospective study was to evaluate the effect of the simultaneous transfer of a low-quality embryo on the implantation and growth of a high-quality embryo and ultimately the live birth rate.

3. Methods

The cross-sectional study was approved by the Dezfoul University of Medical Sciences Ethics Committee (IR.DUMS.REC.1397.005) and performed retrospectively using the referral records of admitted patients in Umm Al-Banin Infertility Treatment Center for IVF/intra cytoplasmic sperm injection (ICSI) procedures from 2013 to September 2020. The required data were extracted from the records and files using relevant checklists. Patients implanting one or two embryos aged 2 or 3 days were included in the study. The records of these patients were classified into four categories:

Group 1: Patients with the transfer of only one grade A embryo

Group 2: Patients with the transfer of two grade A and B embryos

Group 3: Patients with the transfer of two grade A and C embryos

Group 4: Patients with the transfer of two grade B and C embryos

The outcomes included the findings of a chemical pregnancy test (very early miscarriage within the first five weeks of pregnancy), BHCG hormone > 25 IU/L within 14

days after transfer, the number of clinical pregnancies (observation of pregnancy sac in ultrasonography), the number of abortions, the number of multiple conceive fertility and the number of live births (delivery at least 20 weeks after implantation). The quality of embryos was determined as follows: Equal blastomeres without fragmentation (grade A), equal blastomeres with slight fragmentation (grade B), and unequal blastomeres with or without fragmentation (grade C). Additional information in the patient files was also recorded, including the cause of infertility, ova numbers, estradiol levels, transfer date based on cycle, the quality of transferred embryos, chemical pregnancy outcome, clinical pregnancy outcome, abortion numbers, live birth numbers, and multiple pregnancies numbers (pregnancy with more than one fetus). Defective records and lack of accurate information registration were the reasons for the exclusion of the files.

3.1. Statistical Analysis

SPSS version 25 software was used for statistical analysis. The data were analyzed using descriptive statistical parameters, including mean and standard deviation (for quantitative variables) and frequency and percentage (for qualitative variables). The normality of the data was checked by the Kolmogorov-Smirnov test. Also, the Chi-square and one-way ANOVA test was used in the analytical analyses.

4. Results

During the study period (from 2013 to September 2020), 1,422 embryo transfer files of patients who were referred to the Dezfoul Infertility Treatment Center for IVF/ICSI procedures were registered. Of these, 802 cases met the inclusion criteria for the transferred embryo qualities. The number of people in each group was as follows:

Group 1: 156 patients with one or two grade A embryos (39.20%)

Group 2: 102 patients with two grade A or grade B embryos (25.63%)

Group 3: 64 patients with two grade A or grade C embryos (16.08%)

Group 4: 76 patients with two grade B or grade C embryos (19.10%)

According to [Table 1](#), the age ranges of women and men participating in this study were 18 - 47 and 23 - 59 years, respectively. The mean age of women and men was 32.52 ± 5.10 and 37.59 ± 6.60 years, respectively. The infertility history of the subjects ranged from 1 to 26 years, with a mean of 6.50 ± 4.55 years. The most important causes of infertility in patients included the male factor in 38.19%, ovarian factor in 19.60%, and polycystic ovary in 28.89% of cases.

Also, in 25.5% of infertility cases, they were multifactorial. Surprisingly, endometriosis, with a frequency of 1.51% was the least common cause of infertility in the research population. Endometrial thickness ranged from 4 to 11 mm, with a mean of 7.90 ± 1.01 mm.

Concerning the characteristics of the ovarian cycle in patients (Table 2), estradiol levels ranged from 375 to 11632, with a mean of 2955.37 ± 2128.93 . The number of recovered oocytes ranged from 1 to 24, with a mean of 6.84 ± 4.43 . The number of adult ova in metaphase II ranged from 1 to 20, with a mean of 5.72 ± 3.63 , the number of follicles was reported from 1 to 24, with a mean of 6.50 ± 4.28 , and the number of embryos ranged from 1 to 20, with a mean of 4.05 ± 2.93 .

Table 3 compares fertility outcomes for the simultaneous transfer of embryos with different qualities. Accordingly, the formation of the embryo's heart was observed in 31 (36.05%), 25 (29.07%), 17 (19.77%), and 13 (15.12%) cases in groups 1 to 4, respectively. These differences were not statistically significant ($P = 0.47$). Fertility results based on pregnancy hormones accounted for 43 (34.68%), 37 (29.84%), 24 (19.35%), and 20 (16.13%) cases in groups 1 to 4, respectively, showing no statistically significant differences ($P = 0.25$). The identified frequencies of chemical abortions in groups 1 to 4 were eight (36.36%), five (22.73%), six (27.27%), and three (13.64%), respectively ($P = 0.13$), while the frequencies of clinical abortions in these groups were four (25%), eight (50%), one (6.25%), and three (18.75%), respectively ($P = 0.27$); there was no significant difference between these groups. The live birth cases were as follows: Group one 25 (33.33%), group two 24 (32%), group three 15 (20%), and group four 11 (14.67%) ($P = 0.26$). Multiple pregnancy cases were five (33.33%), six (40%), two (13.33%), and two (13.33%) in groups 1 to 4, respectively. The chi-square test showed that the observed differences were not significant ($P = 0.79$).

5. Discussion

The referral of many patients to infertility treatment centers, which is estimated up to about 15% of the general population, requires planning to provide the necessary conditions for the best possible services in the laboratories of infertility treatment centers. One of the main goals of assisted reproduction methods is to produce embryos with the highest quality, which has always been a challenge for experts in this field (10). Our study was designed based on the following questions: What should embryologists do with a low-quality embryo? Should they remove or keep it? Although a low-quality embryo still has a chance of survival, the concern is that in low- and high-quality embryo transfer, the low-quality embryo may harm the high-quality one. Hence, the present retrospective study was

performed to evaluate the success rate of fertility regarding the simultaneous transfer of embryos with different qualities in IVF candidates. Intra cytoplasmic sperm injection was designed and implemented. Out of 1,422 available samples, 802 cases with qualified characteristics in terms of embryo quality and other factors were entered into the study. The grade A and B embryos were considered high-quality embryos, and low-quality embryos were labeled grade C embryos.

The findings indicated that the fertility rate, clinical and chemical abortions, and live and twin birth rates were not significantly different between the groups. Hill et al. evaluated the fertility rates for transmitted embryos with different qualities. In their retrospective study, 4,640 patients who had in vitro fertilization were analyzed, and the findings revealed that the transfer of the second embryo with lower quality had no negative impact on the live birth rate, which is consistent with the present results. However, this study showed that the transfer of the second, low-quality embryo increased the live birth rate by 10% and the multiple birth rate by 15% (11). However, in the current study, the rate of live birth and multiple births did not show a significant difference between the groups. Aldemir et al. showed that the live birth rate was higher in patients who received two high-quality embryos than in groups that received two embryos of different qualities (12), which is inconsistent with the present results that indicated no significant effect due to the simultaneous transfer of two high-quality embryos, i.e., grade A-A and A-B embryos.

Li et al. assessed the impact of low-quality embryos on high-quality embryos in concomitant transfer cases and approved no significant difference in pregnancy and live birth rates between patients in the two study groups, but the pregnancy rate for twins and multiples was significantly higher in cases of concomitant low/high-quality embryo transfer (13). There was no significant difference concerning the birth rate of multiples between different groups. Similarly, in a study by Oron et al., no differences were observed concerning abortion rates and pregnancy complication rates for the mother and the fetus (5). In contrast, Tao et al. stated that the transfer of a low-quality embryo would harm the high-quality embryo (14). Two other researchers also investigated the issue, and both confirmed that low- and high-quality embryo transfer could reduce implantation and fertility rates. However, these researchers did not report any differences in terms of clinical pregnancy rates, live birth rates, abortion rates, abnormal pregnancy rates, or multiple pregnancies, which is consistent with the current findings (15, 16).

Table 1. Demographic Parameters of the Study Groups

Variables	Group 1	Group 2	Group 3	Group 4	P-Value
Female age (y)	32.86 ± 4.72	32.44 ± 5.49	32.12 ± 4.85	32.30 ± 5.56	0.74
Male age (y)	37.25 ± 5.97	37.38 ± 7.14	38.32 ± 6.46	37.96 ± 7.22	0.67
Duration of infertility (y)	6.52 ± 4.26	6.56 ± 4.49	6.60 ± 4.64	6.31 ± 5.24	0.97
Cause of infertility					
Male factor	31.23 ± 3.29	29.34 ± 4.12	33.45 ± 2.39	34.56 ± 4.38	0.75
Female factor	26.42 ± 2.13	24.34 ± 5.70	32.72 ± 3.45	29.43 ± 3.21	0.68
Both	24.42 ± 3.2	32.31 ± 4.3	28.56 ± 3.65	35.77 ± 4.83	0.72
Endometrial diameter (mm)	7.85 ± 1.04	7.92 ± 0.93	7.91 ± 0.97	7.99 ± 1.03	0.83

Table 2. Characteristics of the Ovarian Cycle of the Study Groups

Variables	Group 1	Group 2	Group 3	Group 4	P-Value
Estradiol level (pg/mL)	2852.90 ± 2155.22	3045 ± 2232.55	2731.89 ± 1721.37	3233.53 ± 2245.83	0.46
Oocyte number	6.55 ± 4.31	6.73 ± 4.41	7.39 ± 4.49	7.13 ± 4.47	0.56
Mature oocyte (MII)	5.43 ± 357	5.74 ± 3.76	6.29 ± 3.69	5.82 ± 3.51	0.45
Follicle number	6.28 ± 4.26	6.65 ± 4.31	6.71 ± 4.11	6.57 ± 4.47	0.86
Embryo number	3.64 ± 2.86	4.21 ± 3.09	4.39 ± 2.80	4.40 ± 2.93	0.15

Table 3. Pregnancy Outcomes and Complications in the Study Groups

Pregnancy Outcome	Group 1	Group 2	Group 3	Group 4	P-Value
Clinical pregnancy	80 (26.1)	48 (22.5)	27 (27.8)	35 (18.8)	0.2
Biochemical pregnancy	114 (37.3)	72 (33.8)	34 (35.1)	49 (26.3)	0.09
Chemical abortions	16 (5.2)	11 (5.2)	7 (7.2)	7 (3.8)	0.66
Clinical abortions	18 (5.9)	12 (5.6)	1 (1)	9 (4.8)	0.27
Live births	72 (23.5)	43 (20.2)	23 (23.7)	28 (15.1)	0.12
Multiple pregnancies	2 (3.7)	6 (14)	3 (13.6)	3 (10.7)	0.78

5.1. Conclusions

The findings showed that pregnancy outcomes, including fetal heart formation, hormonal indices, multiple birth rates, chemical, and clinical abortions, and live birth rates, were not significantly associated with the simultaneous transfer of embryos with different qualities. Accordingly, the fertility success rate is not possibly affected by the simultaneous transfer of embryos with different qualities in IVF/ICSI candidate patients. However, due to the lack of sufficient studies, further research is recommended at other infertility treatment centers to obtain more accurate results by comparing achievements.

Acknowledgments

The authors would like to acknowledge Dezful University of Medical Sciences for its financial support.

Footnotes

Authors' Contribution: S. M. P. and S. J. contributed to the conception and design. S. M. P. and S. M. contributed to all experimental work, statistical analysis, and interpretation. S. M., S. J., and M. A. B. were responsible for overall supervision. S. M. drafted the manuscript, which was revised by S. M. P., S. J., and M. A. B. All authors read and approved the final manuscript.

Conflict of Interests: There are no competing financial interests. Sima Janati is a member of the editorial board of Trends in Medical Sciences journal and contributed to the conception and design. She was responsible for overall supervision. Behmanesh is Poormoosavi's husband.

Ethical Approval: The cross-sectional study was approved by Dezful University of Medical Sciences Ethics Committee (IR.DUMS.REC.1397.005). Link: ethics.research.ac.ir/IR.DUMS.REC.1397.005.

Funding/Support: Dezfoul University of Medical Sciences.

References

- Ramezani M, Ashtiyani S, Shamsi M, Taheri S. [The opinion and views of Rhaze's, Avicenna's, and Jorjani's views on fertility and infertility]. *Complement Med J*. 2013;**3**(2):504-15. Persian.
- Hosseini J, Emadedin M, Mokhtarpour H, Sorani M. [Prevalence of Primary and Secondary Infertility in Four Selected Provinces in Iran, 2010-2011]. *Iran J Obstet Gynecol Infertil*. 2012;**15**(29):1-7. Persian. <https://doi.org/10.22038/ijogi.2012.56>.
- Khalili MA, Razavi V, Mardanian F, Esfandiari N. The predictive value of pronuclear morphology screening on embryo development and pregnancy outcome in ART cycles. *Middle East Fertil Soc J*. 2008;**13**(1):44-51.
- Quenby S, Vince G, Farquharson R, Aplin J. Recurrent miscarriage: a defect in nature's quality control? *Hum Reprod*. 2002;**17**(8):1959-63. [PubMed ID: 12151421]. <https://doi.org/10.1093/humrep/17.8.1959>.
- Oron G, Son WY, Buckett W, Tulandi T, Holzer H. The association between embryo quality and perinatal outcome of singletons born after single embryo transfers: a pilot study. *Hum Reprod*. 2014;**29**(7):1444-51. [PubMed ID: 24812313]. <https://doi.org/10.1093/humrep/deu079>.
- Niinimäki M, Veleva Z, Martikainen H. Embryo quality is the main factor affecting cumulative live birth rate after elective single embryo transfer in fresh stimulation cycles. *Eur J Obstet Gynecol Reprod Biol*. 2015;**194**:131-5. [PubMed ID: 26366790]. <https://doi.org/10.1016/j.ejogrb.2015.08.031>.
- Roberts SA, McGowan L, Mark Hirst W, Vail A, Rutherford A, Lieberman BA, et al. Reducing the incidence of twins from IVF treatments: predictive modelling from a retrospective cohort. *Hum Reprod*. 2011;**26**(3):569-75. [PubMed ID: 21163856]. <https://doi.org/10.1093/humrep/deq352>.
- Paria BC, Dey SK. Preimplantation embryo development in vitro: cooperative interactions among embryos and role of growth factors. *Proc Natl Acad Sci U S A*. 1990;**87**(12):4756-60. [PubMed ID: 2352946]. [PubMed Central ID: PMC54196]. <https://doi.org/10.1073/pnas.87.12.4756>.
- Ferraretti AP, Goossens V, de Mouzon J, Bhattacharya S, Castilla JA, Korsak V, et al. Assisted reproductive technology in Europe, 2008: results generated from European registers by ESHRE. *Hum Reprod*. 2012;**27**(9):2571-84. [PubMed ID: 22786779]. <https://doi.org/10.1093/humrep/des255>.
- Papanikolaou EG, Kolibianakis EM, Tournaye H, Venetis CA, Fatemi H, Tarlatzis B, et al. Live birth rates after transfer of equal number of blastocysts or cleavage-stage embryos in IVF. A systematic review and meta-analysis. *Hum Reprod*. 2008;**23**(1):91-9. [PubMed ID: 17965420]. <https://doi.org/10.1093/humrep/dem339>.
- Hill M, Eubanks AE, Csokmay JM, Christy AY, Jahandideh S, DeCherney AH, et al. Is transferring a lower-quality embryo with a good-quality blastocyst detrimental to the likelihood of live birth? *Fertil Steril*. 2020;**114**(2):338-45. [PubMed ID: 32624214]. <https://doi.org/10.1016/j.fertnstert.2020.03.027>.
- Aldemir O, Ozelci R, Baser E, Kaplanoglu I, Dilbaz S, Dilbaz B, et al. Impact of Transferring a Poor Quality Embryo Along with a Good Quality Embryo on Pregnancy Outcomes in IVF/ICSI Cycles: a Retrospective Study. *Geburtshilfe Frauenheilkd*. 2020;**80**(8):844-50. [PubMed ID: 32817991]. [PubMed Central ID: PMC7428370]. <https://doi.org/10.1055/a-1213-9164>.
- Li J, Du M, Zhang Z, Guan Y, Wang X, Zhang X, et al. Does a poor-quality embryo have an adverse impact on a good-quality embryo when transferred together? *J Ovarian Res*. 2018;**11**(1):78. [PubMed ID: 30180866]. [PubMed Central ID: PMC6122748]. <https://doi.org/10.1186/s13048-018-0452-6>.
- Tao T, Robichaud A, Mercier J, Ouellette R. Influence of group embryo culture strategies on the blastocyst development and pregnancy outcome. *J Assist Reprod Genet*. 2013;**30**(1):63-8. [PubMed ID: 23239126]. [PubMed Central ID: PMC3553343]. <https://doi.org/10.1007/s10815-012-9892-x>.
- Pandian Z, Marjoribanks J, Ozturk O, Serour G, Bhattacharya S. Number of embryos for transfer following in vitro fertilisation or intracytoplasmic sperm injection. *Cochrane Database Syst Rev*. 2013;**2013**(7). CD003416. [PubMed ID: 23897513]. [PubMed Central ID: PMC6991461]. <https://doi.org/10.1002/14651858.CD003416.pub4>.
- Demirel C, Goksever Celik H, Tulek F, Tuysuz G, Donmez E, Ergin T, et al. The impact of a poor quality embryo on the implantation chance of a good quality one when transferred together: A study on double blastocyst transfers. *J Gynecol Obstet Hum Reprod*. 2021;**50**(6):101967. [PubMed ID: 33161131]. <https://doi.org/10.1016/j.jogoh.2020.101967>.