

## Specialists' Attitude toward Appropriate Number of Transferable Embryos in Assisted Reproductive Technology in Iran

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### Abstract

**Background:** In recent years, the high likelihood of the implantation of transferred embryos has led to an increase in the number of multiple pregnancies and consequently an increased risk of complications in fetuses and mothers. Since the aim of infertility treatment is the birth of a healthy child while preserving the mother's health, therefore, attempts should be made to avoid multiple pregnancies as much as possible besides maintaining the women's chance of pregnancy by transferring an appropriate number of embryos.

**Methods:** The population under study consisted of specialists (gynecologists and embryologists) who worked in ART clinics across the country and had attended an infertility congress in Tehran in 2008. The devised questionnaire enquired about the infertility specialists' attitude towards the appropriate number of transferable embryos. The questions were designed on a Likert scale of strongly agree, agree, indifferent, disagree and strongly disagree. The scores of the questionnaire ranged from 0–60 which were later scaled up to 100 for ease of data analysis. Accordingly, scores below 50 were considered as “negative”, 50–75 “moderate” and greater than 75 as “positive”.

**Results:** Overall, 9.9% of the specialists gained a score less than 50 (negative view), 67.3% between 50–75 (moderate) and 22.8% greater than 75 (positive view).

**Conclusion:** The infertility specialists in Iran are relatively reluctant to transfer a high number of embryos for infertility treatments.

**Keywords:** Assisted Reproductive Technology, Complications, Embryo, Multiple pregnancy, Specialists, Transfer.

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### Introduction

Since the birth of the first IVF (in vitro fertilized) baby in 1978, the possibility of pregnancy and having a child through Assisted Reproductive Technology (ART) was provided for many infertile couples. However, this achievement brought about multiple pregnancies as a result of ovarian stimulation, and transfer of a large number of embryos to increase the success rate.

According to the data, the use of ART has led to multiple pregnancies in 32% of the cases in USA (1), 23% in Europe (2) and 17% in Australia (3).

At the beginning, a considerable number of embryos ( $\geq 4$ ) were transferred as the success rates of embryo implantation and subsequent pregnancy were low. In recent years, the high likelihood of embryo implantation due to improved ovarian

stimulation methods, suitable condition of embryo culture, possibility of selecting high-quality embryos, and ideal uterine preparation, have shed serious doubts on the maximum number of transferred embryos. High embryo implantation rates have led to increase in the number of multiple pregnancies (4); for example, the use of ART increased the rate of multiple pregnancies by 41% in England between 1995 and 2003 (5). Moreover, the increase in adverse effects and mortality rate of pregnant mothers, embryos and babies during multiple pregnancies compared with single ones on one hand (6–8) and considerable increase in the related costs on the other, has raised the attention of specialists to prevent these medical effects (9).

In countries with high rates of pregnancy, having a child is particularly important for couples and their families because of social and cultural reasons (10); therefore, infertile couples request more embryos to be transferred to increase the success rate of pregnancy, regardless of the difficulties associated with multiple pregnancies such as low birth weight, the high mortality rate of fetuses, hospitalization of the newborns and increased maternal complications (11). Since the aim of infertility treatment is the birth of a healthy child while preserving the mother's health, therefore, besides maintaining the women's chance of pregnancy by transferring the appropriate number of embryos, attempts must be made to avoid multiple pregnancies as much as possible.

Nowadays, some KAP<sup>1</sup> studies have been conducted all over the world to evaluate attitude and awareness of infertility specialists regarding various issues raised by employing ART procedures. However, in Iran there are few studies focusing particularly on the attitude and views of infertility specialists and infertile couples towards an appropriate number of transferable embryos. Due to the lack of legal restrictions on the number of transferred embryos or a regulatory body to oversee the work of infertility clinics as well as the possibility of eliminating selected embryos, the number of multiple pregnancies has increased. On the other hand, the increasing cost of hospitalization (related to the adverse effects of large number of transferred embryos) has raised concerns for the country's health system. Unfortunately, clients realize the problem just after encountering it. However, the consultations offered by infertility

treatment specialists in some clinics could modify the clients' expectation for transferring more embryos. Assessing the attitude of reproductive specialist could help policy makers develop more appropriate treatment guidelines, something which could benefit all parties in the long-run.

### Methods

This study was performed in Avicenna Research Institute in Tehran, Iran. A questionnaire was designed based on studying the related literature and reviewing the relevant questionnaires in accordance with the country's standards of reproductive health. It consisted of 23 questions which inquired about infertility specialists' attitude toward the appropriate number of transferable embryos.

The questionnaire contained questions on age, sex, specialty, work experience in infertility treatment, inclusion of the clients in decisions about the number of transferable fetuses in one cycle, inquiry about the person who made the final decision on the appropriate number of transferable fetuses, the minimum and maximum number of transferable fetuses, the appropriate number of transferable fetuses from the specialists' view, existence of a definite law on the number of transferable fetuses, quantity effects of transferable fetuses on success rate, transfer of a single fetus in optimal condition of the couples, use of fetal reduction methods in multiple pregnancies, financial burden of higher numbers of transferable fetuses on fertility centers and the clients, and the attitude of the specialists on the coverage of infertility treatment costs by insurance companies.

The questions were designed on a Likert scale of strongly agree, agree, indifferent, disagree and strongly disagree responses. The scores were from 0–60 which were later scaled up to 100 for data analysis. Accordingly, scores of less than 50 were considered as “negative”, 50–75 “moderate” and greater than 75 as “positive” attitude. A pilot study was done on experts of related fields of embryology, obstetrics and gynecology to validate the test. For reliability analysis, the questionnaires were completed by 11 specialists attending a laparoscopy workshop at Avicenna Infertility Clinic in 2008, and in revision of the final study, we achieved a Cronbach Alpha of 0.71.

The final questionnaire was filled out by 101 specialists, (80 gynecologists and 21 embryologists) who worked in ART clinics across Iran and had attended the fifteenth congress of Iranian So-

1- Knowledge, Attitude and Practice

**Table 1.** Relative and absolute frequency distribution of specialists' attitude based on the involvement of patients' decision about the number of embryos for transfer

Involvement of patient's decision about number of embryos	Very high	High	Moderate	Low	Very low	Without patient involvement	Total
	Count (%)	Count (%)	Count (%)	Count (%)	Count (%)	Count (%)	Count (%)
	10 (9.9)	26 (25.7)	36 (35.6)	19 (18.8)	5 (5)	5 (5)	101 (100)

ciety of Reproduction and Infertility in February 2008.

After collecting the data, the results including the relationship between the specialists' experience in the field of infertility treatment and all other questions related to their views were analyzed using SPSS version 11.5 through descriptive analyses, the non-parametric test of Mann-Whitney, Kruskal-Wallis, and Spearman's rank correlation coefficient. A p-value less than 0.05 was considered significant.

### Results

The results of this study indicated that 87.1% of 101 infertility specialists had experience in the field for over 2 years.

The lowest total score was 40 and the highest was 86.67 while the mean total score was 65.14±10.3. Overall, 9.9% of the specialists gained a score of less than 50 (negative attitude), 67.3% gained a score between 50–75 (moderate) and 22.8% scored greater than 75 (positive attitude).

Overall, 35.6% of the specialists agreed with the provision of consultation to help clients make decision on the number of embryos for transfer.

On decision about the number of embryos for transfer, 42.6% of the specialists chose the option "absolutely the medical team's responsibility" and 41.6% chose the option "after adequate explanation it is the client's responsibility".

ation it is the client's responsibility".

In this study, 44.6% of the specialists believed that the clients must be the main decision makers on the number of embryos for transfer "after being given the required information", while 53.5% of the specialists believed that the medical team should be the main decision maker "without providing further information to the clients" (Table 1).

The question on the participants' medical experience in transferring a single embryo despite the availability of a number of suitable embryos and the lack of restriction on the issue revealed that more than half of the specialists (56.7%) had not practiced so in contrast to 41.6% with the experience. 43.6% of the specialists had transferred a maximum of three embryos to 20–30 years-old clients (Table 2), whilst 41.6% had worked on at least one embryo transfer (Table 2).

This difference was not statistically significant.

There seems to be considerable disparity among specialists concerning the appropriate number of embryos in clients aged 30–40 years. In this study, 41.6% of the specialists recommended that three embryos were the appropriate quantity to be transferred regardless of the patients' age (Table 2). 54.5% of the specialists working in infertility clinics believed internal regulations were needed to monitor the number of embryos to be trans-

**Table 2.** Relative and absolute frequency distribution for the appropriate number of embryos for transfer based on different ages

	1 embryos	2 embryos	2-3 embryos	3 embryos	4 embryos	5 embryos	6 embryos	8 embryos	No answer	Total
	Count (%)	Count (%)	Count (%)	Count (%)	Count (%)	Count (%)	Count (%)	Count (%)	Count (%)	Count (%)
The maximum number of embryos transferred to 20-30 year-old patients	--	12 (11.9)	--	44 (43.6)	28 (27.7)	6 (5.9)	4 (4)	--	7 (6.9)	101 (100)
The minimum number of embryos transferred to 20-30 year-old patients	42 (41.6)	36 (35.6)	--	7 (6.9)	3 (3)	--	--	--	13 (12.9)	101 (100)
The maximum number of embryos transferred to 30-40 year-old patients	--	5 (5)	--	15 (14.9)	39 (38.6)	18 (17.8)	12 (11.9)	2 (2)	10 (9.9)	101 (100)
The minimum number of embryos transferred to 30-40 year-old patients	29 (28.7)	24 (23.8)	--	25 (24.8)	6 (5.9)	--	1 (1)	--	16 (15.8)	101 (100)
The appropriate numbers of embryo to transfer	--	39 (38.6)	3 (3)	42 (41.6)	14 (13.9)	--	--	--	3 (3)	101 (100)

**Table 3.** Relative and absolute frequency distribution according to study questions

Questions	Strongly agree	Agree	Indifferent	Disagree	Strongly Disagree	Total
	Count (%)	Count (%)	Count (%)	Count (%)	Count (%)	Count (%)
Increase the success rate of pregnancy with high numbers of transferable embryos	7 (6.9)	27 (26.7)	25 (24.8)	39 (38.6)	3 (3)	101 (100)
1-2 embryo transfer with high likelihood of pregnancy	41 (40.6)	45 (44.6)	5 (5)	9 (8.9)	1 (1)	101 (100)
Higher numbers of embryo transfer and acceptance of multiple pregnancies despite good quality embryos and uterine conditions and younger age	2 (2)	14 (13.9)	15 (14.9)	54 (53.5)	16 (15.8)	101 (100)
Single embryo transfer with good quality embryos, good uterine condition and younger age	23 (22.8)	36 (35.6)	19 (18.8)	21 (20.8)	2 (2)	101 (100)
Low numbers of embryo transfer and embryo freezing	47 (46.5)	40 (39.6)	9 (8.9)	5 (5)	0 (0)	101 (100)
Higher numbers embryo transfer and embryo reduction in cases of multiple pregnancies	6 (5.9)	21 (20.8)	20 (19.8)	42 (41.6)	12 (11.9)	101 (100)

**Table 4.** The correlation between the specialists' attitude score with other variables

Specialists' attitude score	Correlation coefficient (Spearman)	P-value
Age	0.13	0.2
Work history of the infertility specialist	0.08	0.41
Decision-making for embryo transfer	-0.1	0.28
Appropriate number of embryo to transfer	-0.19	0.054

ferred in their workplace (Table 3). Overall, 50% of the gynecologists disagreed with the request of clients for more embryo transfer.

85.2% of the specialists believed that transfer of one or two embryos would increase the success rate. 53.5% of the specialists opposed the transfer of multiple embryos and subsequent reduction of them as a method in the case of multiple pregnancies (Table 3). On the contrary, 59.4% of the specialists were in disagreement to restrict the number of transferable embryos to one or two, because they believed it contributed to lower pregnancy success rates and higher costs for the clients.

There was a negative correlation between the specialists' work experience and their views on more embryo transfers to enhance the success rate. However, this relationship was not statistically significant (Table 4). Moreover, the relationship between the specialists' attitude and the ultimate decision maker on the appropriate number of embryos was analyzed by Kruskal Wallis test, and no significant statistical relationships were found.

### Discussion

Unpublished statistics indicate that out of 495 pregnancies in Avicenna Infertility Clinic, 30.82% have been twin pregnancies and 2.15% triple ones. The relatively low rate of triple pregnancies could be due to the internal regulations and guidelines in the Clinic.

In the present study, the gynecologists and embryologists had positive views regarding the transfer of a single embryo and a high rate of pregnancy in young clients. However, only 41.6% of the specialists had such an experience. Moreover, most of the participant (69.3%) disagreed with the idea that the presence of favorable uterine conditions, good quality of embryos, and the couple's younger age could increase the rate of multiple pregnancies by transfer of a high number of embryos.

Reports of increasing hospital costs, side-effects and problems associated with the transfer of a high number of embryos in pregnancies resulting from ART have raised concern for the public health system and need policy makers' due attention. Unfortunately, clients usually realize dimensions of the complications and financial burdens just after experiencing multiple pregnancies; (there have been reports of up to six babies in a single delivery) (12).

The opening of discussions such as the maximum number of embryos for transfer or the higher number of transferable embryos increase pregnancy and birth rates at a cost emphasize the point that infertility specialists are relatively reluctant to transfer a high number of embryos in Iran. There-

fore, they have set some restrictions in their relevant clinics and try to provide adequate information to guide the clients better decide on the number of embryos. However, some cases of multiple pregnancies through ART have been reported. The idea of establishing self-regulatory restrictions on the transfer of embryos has been achieved by more than 20 years of experience among specialists who have been the source of information in this study. It seems the overall atmosphere is appropriate for developing national guidelines by the authorities. In the present study, there was a positive outlook amongst the majority of specialist (85.2%) towards the transfer of one or two embryos with high likelihood of success. Koivurova et al. reported that multiple pregnancies increased the health care costs and therefore, prevention of multiple pregnancies was the most effective method for reducing the costs of IVF (13). Peperstraten et al. stated that in countries where there existed medical insurance coverage for infertility treatments, the number of transferred embryos was critical for most insurance companies. Accordingly, they do not cover clinics where transfer of high numbers of embryos is practiced, because they believe the possibility of side-effects related to infertility treatments is high in these centers (14). Studying specialists' view on the effects of multiple embryo transfer on increasing or decreasing the patients' financial burden showed that the transfer of one or two embryos would not impose too much financial burden on the patients.

In this study, specialists had positive views on infertility insurance coverage and only 4% opposed it. It seems that by the implementation of infertility insurance coverage, most infertility specialists would agree with the transfer of one or two embryos in every cycle in Iran.

Achieving the desired goals necessitates adoption of policies that help reduce the psychological and physical pressure of infertility such as inattention to the related social and cultural pressures for higher pregnancies, prioritization of the mother's and child's health, coverage of the total costs of diagnosis and treatment, giving awareness to the clients to repeat the treatment procedure whenever necessary and giving information about the possibility of freezing and preserving the surplus embryos for the next cycles to prevent physical harm or financial loss. All these factors help the clients make better decision on the number of transferable embryos.

Berin et al. discovered that transfer of 2 instead of 3 frozen embryos in clients below the age of 35 clearly reduced the rate of multiple pregnancies without any effects on the success rate.

This study revealed that gynecologists and embryologists had a positive outlook towards transfer of fewer number of embryos and freeze of surplus embryos at the same time (15). This positive view along with the opportunity to freeze embryos instead of transferring all of them ensures the possibility to repeat the procedure with less expense and provide the basis for transfer of a limited number of embryos in such procedures in the country.

The cause of infertility, embryo quality, client's age, history of treatment and uterus conditions are scientifically critical factors in determining the appropriate number of embryos for transfer in every cycle. It seems restricted rules and regulations on the transfer of a certain number of embryos currently applied in some European countries seem not to have a comprehensive basis and these measures restrict individuals who medically need more embryos.

Guidelines should consider both the patients' interest and the competency of the procedure, such as those done in the USA and Canada which seem to be helpful in this regard. In the present study, 54.5% of the specialists stated that some regulations had been established regarding the number of transferable embryos in their relevant clinics. It is worth noting that setting out comprehensive guidelines can provide an appropriate basis for a similar practice in infertility clinics in the country.

Lee et al. stated that quality of embryos and the patients' age can be essential factors in determining the number of transferable embryos, respectively in young and middle-aged clients (16).

Whilst Berkowitz et al. pointed out that pregnancies resulting from ART have led to triple and/or more pregnancies, embryo reduction is the only logical way for cases with only this option. Otherwise, they have accepted the risk of early birth and/or dangers of continuing pregnancy (17). According to this study, it appears that the number of embryos transferred in Iranian clinics is much higher than those of the developed countries which might be due to some various factors such as quality of services, lack of comprehensive guidelines, insufficient experience of some specialists, lower chances of successful pregnancy in the absence of such measures, superiority of preg-

nancy over successful delivery in the general belief, lack of access to skilled embryologists along with gynecologists in infertility treatment centers, lack of advanced laboratory equipment and/or lack of quality control in the laboratories compared to the ones in developed countries.

### Conclusion

Evaluating the attitude of specialists towards the use of embryo reduction method in order to avoid multiple pregnancies was the subject of this study. In this respect, most of the gynecologists and embryologists reckoned that embryo reduction was an effective method in reducing multiple pregnancies. Moreover, there were no positive views regarding the transfer of a high number of embryos and employing embryo reduction method when multiple pregnancies occur.

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