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## Comparison of fresh embryo donation results in azoospermic couples with embryo transfer in tubal factor infertility

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# Comparison Of Fresh Embryo Donation Results In Azoospermic Couples With Embryo Transfer In Tubal Factor Infertility

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## Table of Contents

- Introduction
- Materials and Methods
- Results
- Discussion
- Conclusion
  - Acknowledgement
  - Correspondence to

## Abstract

**Background and objective:** In Iran sperm donation is prohibited for azoospermic infertile couples, so our objective was to compare fresh embryo donation results in azoospermic couples with embryo transfer in tubal factor infertile couples. **Material and Methods:** A retrospective study was conducted on two hundred twenty five women in a private infertility center. Fresh embryo donation and their comparison group consisted of 158 and 67 patients, respectively. Donors (women with tubal factor infertility), entered the stimulation cycle; simultaneously, endometrium of the recipients (women with azoospermic husband), were prepared by hormonal drugs. After transvaginal, ultrasound guided oocyte retrieval and intracytoplasmic sperm injection (ICSI); fresh embryo (2days after fertilization) was transferred transcervically to the recipient. In tubal factor infertile group the same procedures were performed as the above with the gametes of the genetic parents. Fertilization and implantation rates, chemical pregnancy, and clinical pregnancy were compared between two groups. **Result(s):** Fertilization and implantation rate, clinical pregnancy, chemical pregnancy and blighted ovum were not significantly different between two groups. **Conclusion(s):** We determined that fresh embryo donation has comparable results with embryo transfer in tubal

factor infertile couples. These results support the use of this technique in our society since it prohibits sperm donation.

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## Introduction

Infertility is a major life crisis.<sup>1</sup> It can cause depression, anxiety, social isolation and sexual dysfunction.<sup>2,3</sup> Due to this frustrating experience, many infertile couples seek medical help and finally receive assisted reproductive treatment.<sup>4</sup> Male factor is the only cause of infertility in 20% of infertile couples, but it may be a contributing factor in as many as 30% to 40% of cases.<sup>5</sup> Azoospermia is found among 10% to 15% of infertile men and its classifications consist of pretesticular, testicular, and posttesticular.<sup>6</sup> In testicular azoospermia, therapeutic donor insemination offers an effective option.<sup>7</sup> In Iran, due to serious controversies among Islamic theologians, sperm donation is not permitted, but there is a general consensus that embryo donation could be used as an alternative method.<sup>8</sup>

Embryo donation, despite its many ethical, legal and psychosocial concerns, might indeed be the answer to many infertile couples, who would otherwise have to resort to childlessness or adoption.<sup>9</sup> The first report of embryo donation in assisted reproduction was in 1983.<sup>10</sup> Available evidence indicates that embryo donation success rates globally are high enough to encourage embryo donation as a viable alternative for some infertile couples.<sup>11</sup> A group of couples for whom pregnancy previously was impossible are now delivering babies with high rates of success. This group includes significant male factor infertility and couples with genetic diseases or chromosomal abnormalities.

In some countries embryo donation is prohibited due to social, ethical, legal and religious debates among clinicians, legal scholars and jurists. In our country embryo donation has been accepted since 2003, as an early adoption; which produces a family structure where neither rearing parent is genetically related to the child.<sup>12,13</sup> The advantage over adoption, however, is that the mother would be able to have the pregnancy and, by experiencing it and childbirth, might be able to bond better with the child. The father would also be committed to the child from an earlier stage.<sup>9</sup> Our objective was to compare fresh embryo donation results in azoospermic couples with embryo transfer results in tubal factor infertile couples in our private center. This article may be the first Iranian published research in this regard. Although the legislation about the embryo donation continues to become more perfect and complete, we aimed to depict success rates to encourage embryo donation as an effective and acceptable strategy for some infertile couples.

## Materials and Methods

A total of 225 infertile women were studied retrospectively between 2004 and 2008 at Alvand private infertility hospital in Tehran. After approval of the ethical committee of the Tehran University of Medical Sciences, this study was conducted. The study compared the results of fresh embryo donation in couples with azoospermia of the male partner with embryo transfer in infertile couples with tubal problems of the female partner. All the

azoospermic men had negative testicular biopsy. Tubal factor (tubal ligation or salpingectomy due to previous ectopic pregnancy) infertility was detected by hysterosalpingography. Patients with other causes of infertility were excluded.

In our center, embryo donation is carried out in a manner in which donors are volunteer couples with the history of giving birth to a healthy living child. Female donors are aged between 20-38 years regardless of their husband's age. They were evaluated according to American Society for Reproductive Medicine guidelines including infectious-disease and psychological screening as well as general health and fertility assessment. Donors entered the stimulation cycle at the same time endometrium of the recipient is prepared by hormonal drugs. Transvaginal, ultrasound guided, oocyte retrieval is performed after fertilization through intracytoplasmic sperm injection (ICSI); fresh embryo is transferred transcervically to the recipient. A chart of information data concerning female age, infertility duration, number of transferred embryos, cell number of transferred embryos, grade of embryos, fertilization rate, implantation rate, chemical pregnancy, and clinical pregnancy was completed. All donors and recipients prior to the stimulation cycle received one month treatment with low dose oral contraceptives (Aburaihan Co. Iran,) for cycle synchronization. In the donor group the stimulation protocol for controlled ovarian stimulation consisted of GnRH agonist (Diphereline 3.75 mg, Ferring Co. Germany) half dose, single intramuscular injection in the afternoon of the 21st day of the previous cycle. Recombinant (r) FSH (Gonal F, Serono, Switzerland) 150 IU per day was begun on day 3 of menstruation or later when estradiol was 50 pg/ml. Cycles were monitored using vaginal ultrasound scanning (7.5 MHz transvaginal transducer, Siemens Sonoline G605) and were repeated after 3 days of stimulation. The daily dose of recombinant FSH was adjusted according to the patient's or donor's ovarian response based on the number and size of ovarian follicles as measured by transvaginal ultrasonography. HCG (Pregnyl, Organon) 10000 IU was administered when three or more follicles 17 mm mean diameter were present on ultrasound. Transvaginal, ultrasound guided, oocyte retrieval was performed 34–36 h following the administration of hCG. After fertilization through intracytoplasmic sperm injection (ICSI), embryo was transferred transcervically 2 days later. For all recipients, down-regulation was carried out using a GnRH agonist (Diphereline 3.75mg half dose) injected intramuscularly on the 21st day of the previous cycle. The day that the donor announced the onset of her period, the recipient was informed to have transvaginal sonography examination measuring endometrial pattern and thickness to start Estradiol Valerate (Aburaihan Co. Iran ), 2 mg per day for the first 4 days, 4 mg per day for days 5–8 and 6 mg per day. Estradiol Valerate was continued until the pregnancy test was done and if it was positive, estradiol was continued till 10 weeks of pregnancy. On the day of the oocyte retrieval, 200 mg progesterone (Cyclogest, Actavis Co. UK) was given to the recipient intravaginally and continued with 400 mg, twice daily, until fetal heart beat was observed by ultrasound, then was continued till 10 weeks of pregnancy. Endometrial development was evaluated by ultrasound scan and it was considered mature when the endometrial thickness was 8mm.

In tubal factor infertile group, the stimulation cycle, transvaginal ultrasound guided oocyte retrieval, fertilization through intracytoplasmic sperm injection (ICSI), and transcervical fresh embryo transfer were performed as the above procedures with the gametes of the genetic parents.

A pregnancy test was performed 14 days after embryo transfer, and, if positive, an ultrasound scan was scheduled 2 weeks later to determine the number and status of implanted embryos.

The concurrency of a positive -hCG test and a fetal heart beat (seen by ultrasound) was defined as a clinical pregnancy.

SPSS .13 software (Spss Inc.chicago IL.) was used for data collection and analysis. P value less than 0.05 was considered for statistical significance. Chi square, t test and ANOVA were used for statistical analysis. Data are reported as Means±SD or number (percent).

## Results

Two hundred twenty five women were enrolled in this study with the mean age of 32.1±6.8 (female recipients) in embryo donation group and 30.9±4.8 in embryo transfer group (p=0.004). Infertility duration was 11.1±6.1 years (female recipients) in embryo donation group and 8. 6±4.7 years in the latter group; indicating our patients desire these technologies at later stages of their life (especially in the former group) (table 1). In the embryo donation group, fertilization rate was 63.6±24.6 percent. In the embryo transfer group, fertilization rate was 58.6±30.7 percent. Implantation rate, clinical pregnancy, chemical pregnancy, quality of transferred embryos and blighted ovum were not significantly different between two groups. Blighted ovum was reported in 1.69% of embryo donation group and 2.2% of embryo transfer group.

	Embryo donation N=158	ET in Tubal Factor N=67	P value
Age(years)	*32.1±6.8	30.9±4.8	0.004
Infertility duration(years)	*11.1±6.1	8. 6±4.7	0.158 ns
Fertilization rate	63.6±24.6	58.6±30.7	0.675 ns
Number of transferred embryos	3.3±1.0	3.1±1.1	0.173 ns
Chemical pregnancy	65(41%)	27(39%)	ns
Clinical pregnancy	59(37.3%)	22(32.8%)	0.520 ns
Implantation rate	23.2±15.2%	23.9±14.5%	0.793 ns

Table 1: Comparison of Fresh Embryo Donation with Embryo Transfer results in Tubal Factor Infertility

## Discussion

Religious perspectives on assisted reproductive techniques (ART)s are as varied as the position of secular commentators. At one extreme, the Roman Catholic Church has consistently opposed all forms of ARTs, based on its belief that reproductive must remain inextricably linked to sexual intimacy within a marital relationship.<sup>14</sup> Indeed, some Jewish and Islamic theologians suggest that infertile married couples have a duty to use ARTs, for treatment of infertility. The use of donor gametes (Sperm, oocyte ) and embryo, however are prohibited by many religions.<sup>15</sup>

In Iran, among the majority of Shiite legal authorities in contrast to sperm donation, embryo donation (ED) is an accepted form of assisted reproduction. In this very early adoption; the mother would be able to have the pregnancy and, by experiencing childbirth, might be able to bond better with her child.<sup>13</sup>

Use of the embryos for future pregnancy attempts, donation to other couples or embryo donation agencies, donation to researchers, or thawing and discarding or selling extra cryopreserved embryos are commonly available to the couples.<sup>16</sup> Furthermore, even among couples who need conventional IVF, the significant cost of this treatment, which is often not covered by insurance,<sup>17</sup> may push them toward considering purchasing preexisting embryos because this is a more cost-effective option.<sup>18</sup> The American Society for Reproductive Medicine (ASRM) and the Society for Assisted Reproductive Technology (SART), however, explicitly state that the selling of human embryos is ethically unacceptable.<sup>19</sup>

But due to the lack of legislative regulations and proper guidelines for ART practice in Iran our volunteers may donate their embryos due to either financial reasons or altruistic ideas. Some recipient couples desired known donors, they either selected them or brought them themselves; but the remainders requested anonymous donors. Approximately 90% of embryo donors reported their main motivation was financial problems. In our center, the recipient couples paid all the medical and surgical charges of the donors plus \$400-\$500 for the fresh embryo transfer and for the cryopreserved embryos it was dependent upon the agreement between donors and recipients.

The outcome of an embryo donation program was evaluated. The clinical pregnancy rate in the recipients was 27.8% (15/54) per embryo transfer. An average of 1.9 embryos was transferred on each occasion. The main outcome of our study (pregnancy) was statistically similar between the two groups.

Embryo donation pregnancy and delivery rates vary widely among different nations. All the reasons are not known. Available evidence indicates that ED success rates globally are high enough to encourage ED as a viable alternative for some infertile couples.<sup>11</sup> The implantation and clinical pregnancy rates for fresh donated embryo transfers are higher than for oocyte donation. The use of frozen-thawed embryos may be associated with slightly lower implantation and clinical pregnancy rates compared to fresh embryos.<sup>9</sup> Embryo donation for use by other couples is an attractive option to some patients from these perspectives: first, it is a way for those who believe the embryo represents a human life, yet do not want more children, to avoid the destruction of that life. Second, for the recipients, it is a way to become parents that is less expensive and time-consuming than a conventional IVF cycle—and in most cases, less expensive than traditional adoption.<sup>20</sup> Finally, some parents-to-be are more comfortable having a child who is genetically related to neither parent than to just one of them, as would occur with sperm or oocyte donation.<sup>21</sup> Use of preexisting (surplus) embryos is also less physically intensive than conventional IVF, because undergoing controlled ovarian stimulation and oocyte retrieval could be avoided. However, the problems of the availability and cost of the expertise of preimplantation genetics and also for patients with autosomal dominant disease still make embryo donation a worthwhile consideration.

Some studies have considered the emotional barriers to embryo donation. The interest of the offspring, not only as regards knowing his/her genetic origin but also knowing full-blood genetic siblings, should be kept in mind in embryo donation programs. Embryo donation parents generally knew only the donors' physical characteristics, and thought about and talked

about the donors less frequently than adoptive parents thought about and talked about the birth parents. Embryo donation parents' views on the donors differ from adoptive parents' views on the birth parents, with donors having little significance in family life once treatment is successful.<sup>22</sup> It appears that parental responsiveness rather than biological relatedness is more important in the development of secure attachment relationships, which are central to the emotional well-being of the child.<sup>9</sup>

Clinicians need to raise embryo donation as a possible option, perhaps using educational programs, while media coverage of the issues can educate the general public. In a study of couples' attitudes to embryo disposition after IVF, 52 couples with frozen embryos stored for an average of 4.5 years were interviewed. The most interesting finding was that, for couples who had made a choice both before and after treatment about disposition, only 29% kept the same choice.<sup>23,24</sup>

Fresh embryo donation in our study was scheduled for the specified infertile couples; it may be indicated when surplus embryos are achieved in conventional IVF cycles or the remaining embryos may be cryopreserved for future donations. Although the legislation about the embryo donation continues to become more perfect, many questions remains to be answered; such as the allowed frequency of donations, how much will be the paid costs of donations, and the offspring desire about his genetic knowledge. In many societies which sperm donation is prohibited, embryo donation can be viewed as an effective solution for patients with azoospermic infertility; and other aforementioned situations.

## **Conclusion**

We determined that fresh embryo donation has comparable results with embryo transfer in tubal factor infertile couples. These results support the use of this technique in our society since it prohibits sperm donation.

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