EFFECT OF FRESH AND FROZEN EMBRYO TRANSFER METHOD ON FERTILITY SUCCESS IN ASSISTED REPRODUCTION: A COMPARATIVE STUDY

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ABSTRACT

Objective: To study the fertility success of frozen and fresh embryo transmission methods.

Methodology: In this descriptive study, 307 infertile women selected by convenience sampling who were referred to the infertility treatment center of Besat Hospital, Sanandaj, Iran from 2015 to 2016 were treated by intra-cytoplasmic sperm injection. In total, 231 patients received fresh embryos and 76 patients received frozen ones. The results of b-HCG, sonography, miscarriage, and the final result of embryo transfer were analyzed by SPSS software using t-test for quantitative outcomes and Fisher's test and chi-square for qualitative outcomes.

Results: The transfer of frozen embryo was more successful than fresh embryo transmission. However, it was not a statistically significant difference (p= 0.16). Besides, the difference in biochemical (p= 0.21) and clinical pregnancy (p= 0.53) between the two methods used to produce fertility was not significant. However, the miscarriage rate in the fresh form of transfer was lower than in the frozen one (p= 0.04).

Conclusion: No difference was found in biochemical and clinical pregnancy between frozen and fresh transfer methods. However, the miscarriage rate was more in the frozen transmission.

Key Words: Embryo transfer, Fertility, Pregnancy

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INTRODUCTION

Infertility is a worldwide and very common problem in reproductive health. No less than 15% of couples experience infertility in their fertility ages all over the world[1]. Female factors are responsible for 65% of the causes of infertility. More than 80% of the causes of infertility in women are due to ovulation dysfunctions and abnormalities in the reproductive system. Also, male factors are responsible for 35% of the causes of infertility[2]. Infertility imposes a lot of psychological and financial burdens on patients and their families. Therapeutic failure will also have psychological effects on the couples. Therefore, using easy, low-cost, and effective treatments is a good choice for the patients[3].

Using assisted reproductive technology (ART) to treat male and female infertility is based on the reproductive rights agenda established at the International Conference on Population and Development (ICPD) held in Cairo 15 years ago[4]. The transfer of embryo is a highly effective way to obtain fertility. By 'embryo transfer' is meant a stage in the course of assisted reproduction in which embryos are planted into the uterus of a female person with the aim of inducing a pregnancy[5]. Embryos are either "fresh" from fertilized oocyte cells of the same menstrual cycle, or "frozen". Researchers have shown successful pregnancies resulting from eggs that people have stored for up to 10 years. There are no long-term researches on embryo freezing since doctors have been performing the procedure only since 1983[6]. The frozen method was first used for sperm, ovum, and fetus in 1949[7]. The quality of oocyte and sperm, freezing conditions, maintenance status, and uterine conditions are some of the crucial factors affecting the outcome of the fertility method used[8]. Both embryo transfer methods (fresh or frozen) may encounter failure. So far, precise studies have not been done to determine which embryo transfer method (fresh or frozen) is better.

The current research was done to determine the fertility success rates of fresh versus frozen embryo transfer methods.

METHODOLOGY

The study population consisted of 307 infertile patients (selected by convenience sampling) referring to the infertility treatment center of Besat Hospital, Sanandaj, Iran from 2015 to 2016. 231 patients received fresh embryos and 76 patients received frozen ones. The protocol for this study was approved (with code RI.MUK.REC 8719) by the Ethics Committee of the School of Medicine of Kurdistan University of Medical Sciences, Sanandaj, Iran. All subjects entered the study with informed consent. A written consent was also received from them.

This descriptive research was conducted to determine the fertility success rate of both frozen and fresh embryo transfer methods. Sampling was done so that all infertile patients referred for embryo transfer were incorporated in the research. In patients with ovarian hyperstimulation syndrome (OHSS) and low endometrial thickness, frozen embryo transfer was carried out, while in the other infertile patients, fresh embryo transfer was done.

The criterion for entering the study was infertile women referred to the infertility treatment center of Besat Hospital, Sanandaj, Iran, from 2015 to 2016. The exclusion criteria included patients with a history of hysteroscopic surgery and patients with a history of endocrine diseases.

The stimulation of ovulation was performed by agonist protocol. With the beginning of the menstrual period, the patients received an anti-pregnancy tablet daily. Gonadotrophin stimulating hormone agonist (Cinfact, Cinagen, Iran) had started at 0.5 ml on the 21st day of the preceding menstrual period. On the 3rd day of the menstrual period, the dose of the agonist was halved, and from days 3 to 7, recombinant gonadotropin (Gonal F) was administered with a dose of 150 to 300 units, according to the amount and age of AMH. Sonography was done on the 7th day of the cycle and gonadotropin dose was determined based on the number of follicles. With the detection of at least 3 follicles larger than 18 mm, chorionic gonadotropin was injected at a dose of 10,000 units, and 36 hours later the oocytes were extracted with spinal anesthesia or mild anesthesia using guided vaginal sonography.

After recovering the follicles, the oocyte was isolated from the cumulus cells using a mechanical technique (pipetting). Then the maturation stages were checked using a microscope. For sperm injection, metaphase II oocytes were placed in a total global culture. An inverted microscope was used for sperm injection. The extruded oocytes were kept in a total global culture in an incubator holding 5% CO2 at 37°C with 98% humidity. The fertilization and formation of pronucleus were investigated after 18 hours. After 72 hours, the embryos (in terms of quality, number, symmetry of blastomeres, and fragmentation rate) were divided into the four degrees of A, B, C, D. The KITAZATO kit was employed to freeze the embryos which were then kept in liquid nitrogen. The KITAZATO kit was utilized to thaw the embryos.

The results of β-HCG, sonography, miscarriage, and the final result of embryo transfer were analyzed by SPSS software. Chi-square test was applied to compare the categorical variables. Differences among the variables of the two ET groups were analyzed using t-test. P <0.05 was considered as the significance level.

RESULTS

The mean age of women was 32.37 ±5.97. Primary infertility was found in 68.4% of the patients who were referred to the Infertility Center and 53.4% of the total patients had a history of using ART without success. For the treatment of infertility, 231 fresh transmissions and 76 frozen transmissions were performed. The demographic characteristics of the patients under study are illustrated in Table 1.

Of the 231 fresh embryos transmitted, 41 positive results were observed; and out of 76 frozen transmissions, 19 were positive (Table 2).

Table 1: Demographic characteristics of patients

Variable	Number of persons	Mean, %
Age (mean ± SEM)	307	32.32 ± 5.97
Husband's Age (mean ± SEM)	307	36.1 ± 6.14
Primary Infertility (percentage)	210	68.4%
Secondary Infertility (percentage)	97	31.6%
Previous Use of ART (percentage)	164	53.4%
Fresh Embryo Transfer (percentage)	231	75.24%
Frozen Embryo Transfer (percentage)	76	24.76%

Table 2: The success rate of embryo transfer

Variable		Embryo Transfer		P Value
		Fresh	Frozen	
Result	Positive	41 (17.7%)	19 (25%)	0.16
	Negative	190 (82.3%)	57 (75%)	

Table 3: Comparison of reproductive consequences in fresh and frozen transmission methods

Variable		Embryo Transfer		P Value
		Fresh	Frozen	
Biochemical Pregnancy	Positive	41 (17.74%)	19 (25%)	0.219
	Negative	190 (82.26%)	23 (75%)	
Clinical Pregnancy	Positive	30 (13%)	12 (15.8)	0.537
	Negative	201 (87%)	64 (84.2%)	
Miscarriage	Positive	16 (6.9%)	12 (15.8%)	0.046

In patients with fresh embryo transfer, the positive biochemical pregnancy rate was 17.74% and clinical pregnancy was 13%; while in patients who had frozen transfusion, these rates were 25% and 15.8% respectively. The miscarriage rate in patients who used the fresh transmission method for fertility was 6.9% which was a significant difference (Table 3).

DISCUSSION

In the current research, the success of frozen embryo transfer was not significantly different from that of fresh embryo transfer in terms of biochemical and clinical pregnancy. However, the miscarriage rate was more in frozen transfer than in fresh transfer. Studies have demonstrated that frozen embryo transfer method increases the risk of high birth weight, preterm delivery, and gestational age[9]. It has been found out that endometrial admission is a highly influential factor on the final result of embryo transfer in both frozen and fresh transfer methods[10,11]. In general, the occurrence of post-pregnancy events in embryo transfer is more than that of normal pregnancy[12]. Both frozen and fresh embryo transfer methods had the same final success rate. Many studies indicate that fertility and pregnancy results are higher in fresh embryos[13]. Others argue that no significant difference exists between these two transmission methods[14]. However, with the advancement of freezing techniques, the chance of pregnancy rose 25 to 50 percent in women who did not have the ability to use fresh embryo transfer method[15]. There are various parameters in these techniques which greatly affect fertility outcomes including endometrial receptivity, a well-balanced embryo endometrium interaction, and the quality of embryo[15].

In this study, the occurrence of biochemical pregnancy in the fresh embryo transfer method was not significantly different from that of frozen embryo transfer method. Based on evidence, the rate of β-HCG in both frozen and fresh methods of embryo transfer increases and is considered an indicator of pregnancy, since in both embryo transfer conditions, the concentration of steroid hormones is critical for admission[16,17]. B-HCG has been reported as a prevalence indicator of chemical pregnancy occurrence in both frozen and fresh transmissions, and it has been stated that the frequency of chemical pregnancy is higher in the frozen transfer method[18].

Clinical pregnancy was more in frozen transmission method than in fresh transmission method. However, no significant difference was noticed between them. Various factors including the level of FSH and highly purified human chorionic gonadotropin (HP-hMG) contribute to clinical pregnancy in frozen and fresh embryo transmission methods[19].

The rate of miscarriage in fresh embryo transfer was significantly lower than that of frozen embryo transfer. Due to the fact that there was no age limit in this study, the high age of some mothers may be one of the influential factors on the incidence of miscarriage in frozen embryo transfer method. 12-15% of normal pregnancies and 18% of pregnancies caused by fertility methods lead to miscarriage before the 20th week of pregnancy[20]. Mandelbaum[21] reported miscarriage rates of 23.24% in the frozen transmission method. Check and colleagues[22] showed that in women with inadequate endometrial thickness, miscarriage due to frozen embryo transfer method was much more prevalent than fresh transfer method. Also, the amount of implantation in frozen transfer was less than that of fresh transfer[23].

CONCLUSION

In the present study, no significant difference in biochemical and clinical pregnancy between the two meth-

ods used to produce fertility was observed. However, the miscarriage rate in the fresh transfer method was lower than that of frozen transfer method. It is recommended that more extensive studies be conducted on different subjects in order to acquire further information regarding the success of frozen or fresh embryo transfer methods during pregnancy as well as the postpartum period.

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CONTRIBUTORS

FS and MR conceived the idea, planned the study, wrote the manuscript, helped analyze the data and appraised the references. AA administered the plan, collected and scrutinized the data and wrote results in light of the objectives. KR critically evaluated the manuscript, reviewed the manuscript and carried out corrections as suggested by reviewers. ZA supervised the study, corrected technical mistakes and liaised with authors. All authors contributed significantly to the submitted manuscript.