

Follow up of infertile patients after failed ART cycles: a preliminary report from Iran and Turkey

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ABSTRACT

Objectives: Assisted reproductive technology (ART) has become an established and increasingly successful form of treatment for infertility. However, significant numbers of cycles fail after embryo transfer (ET) and it becomes necessary to follow up the infertile couples after failed ART treatments. The main goal was to follow up the infertile patients after failed IVF/ICSI+ET treatments in Iran and Turkey.

Study design: 198 infertile couples from Iran and 355 infertile couples from Turkey were followed up after IVF/ICSI failures. The patients' demographic data, the couples' decisions about continuation of treatment and the spontaneous pregnancy rates were compared in the two countries.

Results: The drop-out rate was higher in Iran (28.3%) than in Turkey (23.4%). The reasons for treatment discontinuation in Iran and Turkey were: financial problem (33.9% vs. 41%), hopeless (10.7% vs. 22.9%), fear of drug side-effects (7.1% vs. 12%), achieving pregnancy (37.5% vs. 19.6%), child adoption (5.4% vs. 2.4%), lack of spouse cooperation (5.4% vs. 2.4%), and divorce (0% vs. 2.4%). Spontaneous pregnancy was significantly higher in Iran (10.1%) than in Turkey (3.9%). There was correlation between duration of infertility and female factor infertility with spontaneous pregnancy.

Conclusions: Since the majority of couples that discontinued treatment had financial problems, it is essential for health professionals to support infertile couples during their childlessness crisis.

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1. Introduction

ART treatment has become an established and increasingly successful form of treatment for infertile couples. Despite improvement in the outcomes, IVF and ICSI yield only a 20–25% chance of live birth. Therefore, many infertile couples fail to achieve a child, especially on the first ART attempt [1]. Furthermore, eventual success is not guaranteed, even for infertile couples willing to attempt additional treatment cycles. These obstacles may encourage many couples to stop their ART treatments [1,2]. Therefore, it becomes necessary to follow up the patients after their ART treatment failures. It may assist them to overcome their infertility crisis, either with or without continuation of their treatment programs.

Several studies have reported high rates of dropout from ART programs. Poor prognosis, financial problems and psychological stress contribute to discontinuation of ART treatments [1,2]. Psychological problems, such as depression, are more common in the unsuccessful IVF group than in the successful one [2]. Another important phenomenon to be discussed is the good rates of spontaneous pregnancies after failed infertility therapy, even in cases with male factor infertility [3,4]. Other options that have been elaborated by some are child adoption and gamete or embryo donation after ART failures [5,6]. In this regard, Sydsjö et al. [7] showed that the majority of their unsuccessful IVF couples discussed adopting children.

Although there have been extensive research studies on the follow up of infertile patients as well as the factors involved in discontinuation of treatment after failed ART cycles in different societies, no report has been published from Muslim societies yet. Therefore, the goal of this study was to follow up infertile couples after failed ART cycles in the Islamic societies of Iran and Turkey. A deeper understanding about the infertile couples' situations during their ART failure would help specialists to offer them more success and hopefully a better life.

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2. Materials and methods

This descriptive study was designed to follow up the infertile patients who failed ART cycles at the university-affiliated Institute for Reproductive Sciences in Yazd, Iran, and the ART and Genetics Center in Istanbul, Turkey during the years 2009–10. Both are considered major referral centers for infertility in respective countries. The inclusive criteria were: (1) presence of complete treatment files; (2) patients who underwent either IVF or ICSI only; and (3) patients who were successful up to the ET technology but failed afterwards (no pregnancy reported). In Iran, a total of 251 infertile patients were selected for this survey. However, only 198 cases agreed to participate fully and the rest ($n = 53$) were excluded. The reasons for exclusion were change of residency or lack of valid phone numbers. In Turkey, a total of 370 infertile patients were selected, but 15 couples were excluded. Therefore, a total of 553 cases from both countries were included in this survey.

The participants were divided into two groups, according to their place of infertility treatment, for data analysis. A questionnaire was designed for each case with three sections: (1) collection of demographic characteristics; (2) details of the ART treatment cycles collected from medical records; (3) assessment of their current status after failing ART cycles. The last included a wide range of topics, such as ART attempts at another infertility clinic, spontaneous pregnancies, oocyte or embryo donations, adoption and reasons for discontinuation of ART treatment. In addition, the clinical characteristics of all patients with spontaneous pregnancies after failed cycles were studied in detail. The questionnaires were completed by one staff member of the clinic, by phone.

This study was approved by our university research ethics committee. Statistical comparison between groups was performed by chi-square, independent sample *t*-test and Mann–Whitney test, when appropriate. $P < 0.05$ was considered to be significant.

3. Results

3.1. Demographic information

Demographic data are presented in Table 1. Forty-six (8.13%) patients were over age of 40 years.

3.2. Clinical characteristics

Table 1 shows clinical characteristics of patients. The distribution of infertility etiology between patients in Iran and Turkey was not significant ($P = 0.2$). The rate of secondary infertility was significantly higher in Turkish patients (25.4%) than Iranian (7.6%) (Table 1). The mean number of treatment cycles in Iranian patients was significantly lower than Turkish infertile couples.

3.3. Follow up of failed cases

Dropout rates of treatments were 28.3% and 23.4% in Iran and Turkey respectively ($P = 0.15$). Therefore the majority of patients decided to continue their treatments. However, some of them were undecided about the future treatment plan (3.5% and 7% in Iran and Turkey respectively). Also, referral to other centers was 16.7% in Iran and 1.7% in Turkey. Interestingly, 10.1% and 3.9% of Iranian and Turkish couples conceived naturally after failure of ART cycles ($P = 0.005$) (Table 1).

The reasons for discontinuation of treatment were different in Iran and Turkey ($P = 0.02$). In cases without achieving pregnancy, financial problems were the most important reason (33.9% in Iran and 41% of couples in Turkey). The second important reason was related to “loss of hope”. Other reasons for dropout from ART program were success in spontaneous

Table 1

Comparison between patients' clinical characteristics and treatment discontinuations in Iran and Turkey.

Characteristics	Iran ($n = 198$)	Turkey ($n = 355$)	<i>P</i> value
Woman's age (year)	30.9 ± 5.1	33.97 ± 5.5	0
Duration of infertility (year)	9.78 ± 3.35	8.96 ± 5.5	0.05
No. of embryo transfer	2.38 ± 1.23	2.35 ± 0.85	0.5
No. of treatment cycle	1.78 ± 1.15	2.93 ± 1.90	0
Type of infertility			0
Primary	183 (92.41%)	265 (74.6%)	
Secondary	15 (7.6%)	90 (25.4%)	
Etiology of infertility			0.21
Female factor	111 (56.1%)	179 (50.4%)	
Male factor	87 (43.9%)	176 (49.6%)	
Spontaneous pregnancy	20 (10.1%)	14 (3.9%)	0.005
Discontinuation of treatment	56 (28.3%)	83 (23.4%)	0.15
Reasons for discontinuation			0.02
Refer to other center	33 (16.6%)	6 (1.7%)	0.003
Seeking child adoption	4 (3%)	2 (0.6%)	
Seeking donation	3 (2.3%)	6 (1.7%)	

pregnancy or live birth from a previous ART cycle, fear of drug side effects, planning for child adoption, lack of spouse cooperation during the course of treatment, and divorce (2.4% in Turkey and 0% in Iran) (Fig. 1).

3.4. The characteristics of patients who discontinued treatment

In Iran, no correlation was observed between the woman's age, duration of infertility, numbers of treatment cycles, and etiology of infertility with her decision to stop treatment (Table 2). In Turkey, the duration of infertility in treatment continuation couples (9.19 ± 5.49 years) was more than discontinuation couples (7.95 ± 5.4 ; $P = 0.05$), but other characteristics were not different between the two groups (Table 2).

3.5. Spontaneous pregnancy after failed ART cycles

A total of 20 (10.1%) and 14 (3.9%) Iranian and Turkish couples conceived naturally after failure of treatment cycles (Table 1). The woman's age (Fig. 2) in couples with spontaneous pregnancy and cases who failed was similar (31.41 ± 4.61 vs. 32.98 ± 5.61 years, $P = 0.06$). The majority of patients with spontaneous pregnancy were under age of 35 years. It is important to note that the duration of infertility was significantly less in couples with spontaneous pregnancy than others (6.07 ± 3.9 vs. 9.45 ± 5.74 years, $P = 0$), respectively. In addition, the etiology of infertility in couples with spontaneous pregnancy was different when compared with the failed group ($P = 0.001$). The majority of the pregnant women had female factor infertility (76.5%). In fact, the odds ratio for spontaneous pregnancy among women with female infertility was 2.79.

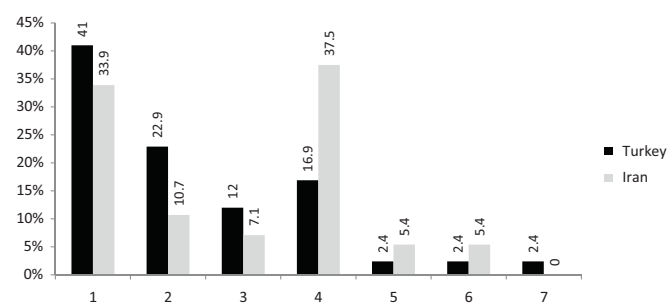


Fig. 1. Reasons for discontinuation of infertility treatment. (1) Financial problem; (2) psychological stress; (3) drug side effects; (4) achieving pregnancy; (5) child adoption; (6) spouse lack of cooperation; (7) divorce.

Table 2

The characteristics of patients who decided to continue or discontinue the ART treatments.

Characteristics	Iran ^a			Turkey ^b		
	Discontinue (n=56)	Continue (n=135)	P value	Discontinue (n=83)	Continue (n=247)	P value
Woman' age (year)	31.25 ± 4.96	30.69 ± 5.23	0.49	33.81 ± 5.60	33.87 ± 5.48	0.93
Duration of infertility (year)	9.24 ± 5.04	9.95 ± 5.46	0.55	7.95 ± 5.40	9.19 ± 5.49	0.054
Number of treatment cycles	1.98 ± 1.31	1.68 ± 1.03	0.15	2.37 ± 1.51	3.06 ± 1.98	0.002
Female factor	27 (49.1%)	56 (58.8%)	0.47	40 (48.2%)	126 (51%)	0.55
Male factor	28 (50.9%)	80 (41.2%)	0.47	43 (51.8%)	121 (49%)	0.55

^a Seven patients were uncertain about their decision on further ART treatment.^b Twenty-five patients were uncertain about their decision on further ART treatment.

3.6. Planning for child adoption or donation

The findings showed that a few patients were seeking child adoption. Only four (3%) couples (40–43 years) in Iran and two (0.6%) (41–43 years) in Turkey adopted a child. Similarly, seeking donation was low in both countries. The results also showed that three (2.3%) couples (27–41 years) in Iran and six (1.7%) couples (25–44 years) in Turkey were interested in donation.

4. Comment

After an unsuccessful ART cycle, an infertile couple's decision to discontinue treatment is probably due to a complex interplay of factors. These include: financial burdens, losing hope, spontaneous pregnancy, psychological stress, drug side effects, divorce, and seeking other options such as child adoption or donation [2,7–9]. Olivius et al. [2] reported that 54% of their infertile couples with failed pregnancies and completing three IVF cycles, decided to discontinue the IVF program. This rate is reported as 70% by Rajkhowa et al. [1] from UK, and 64% by Sharma et al. [9]. Our study showed that the dropout rate from ART program was below 29%, which is much lower than other reports. In this study, financial burden was the first important reason for dropout. Despite the prevalence of infertility, insurance coverage for ART treatment is not available in our societies, and the majority of insurance companies consider infertility as a condition, not a disease. Therefore the cost of infertility diagnosis and treatment is rarely reimbursed to needy patients. Likewise, Rajkhowa et al. [1] reported that lack of personal funding as well as funding from the National Health Service was the main reason for dropout. Therefore, economical problems are considered an important

reason. In another study in the UK, financial constraint was the most important reason for this phenomenon [10]. In France, however, de La Rochebrochard et al. [11] said that the high rates of dropout could not be related to financial crisis, since the first four IVF cycles are fully reimbursed by the insurance system.

Another major factor for discontinuation is “loss of hope” among infertile couples. Filetto et al. [12] stated that losing hope is one of the important reasons for patients to discontinue their treatment cycles. The cause of hopelessness is probably related to the poor prognosis of ART treatment. Poor prognosis was cited by 25% of the discontinued patients in Olivius' study [2]. In another study, 23% of infertile couples reported that lack of IVF success was the main reason for their ART dropout. This factor was strongly associated with psychological stress [1]. Recently, Domar et al. [13] stated that in patients with lack of insurance coverage distress was the primary reason for discontinuing their treatment. Our data showed that hopelessness was the second most important reason for treatment discontinuation in patients with primary infertility. This rate was significantly higher among Turkish couples. It may have to do with the higher treatment expenses in Turkey, or having fewer alternative options such as gamete or embryo donation. In our previous study, we fully discussed that oocyte/embryo donations are legally permissible in Iran [14,15].

Another issue that was surveyed was to determine the role of adoption in couples' decisions. Adoption represents an option for couples after unsuccessful ART treatment to overcome infertility, especially when donation is not allowed in a country [16,17]. Bryson et al. [8] in a follow-up study reported that 21.05% of couples with failed ART treatment had become adoptive parents. In another study in Germany, it was found that 10% of infertile couples applied for adoption [16]. Karpel et al. [6] reported that 18% of infertile couples in France adopted a child. Later, de La Rochebrochard et al. [4] reported that 12% of patients adopted a child. In our study, agreement upon adoption was very low in both societies. It may be due to the long waiting list for adopting a child or fear of the reaction from relatives. Bharadwaj [18] stated that adoption is not an option in India, and their work argued that couples would overcome their problem secretly by accepting donation. Patients generally do not go for the option of adoption that evokes widespread fears of making infertility “visible” in the community. However, the request for donation among infertile couples was found to be low in Iran; despite the general public attitudes and the law being in agreement with this option [14,15]. We did not ask about disagreements with donation and adoption, but apparently this was related to the culture and social attention in these nations. Therefore, it is essential to address the problem in order to introduce adoption issue as an alternative for patients. With regard to this point, Bryson et al. [8] compared women who remained childless after unsuccessful IVF with those who subsequently conceived or adopted. They showed that the former group rated themselves as more stressed, and with a lower life satisfaction and self-esteem. In addition, Soullier et al. [19] confirmed that the woman's age is an important factor in patients' decision to discontinue their treatment, though we did not find any

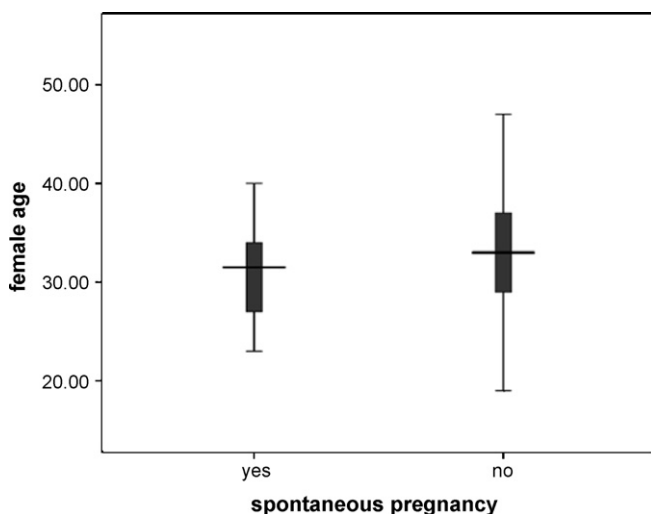


Fig. 2. Age distribution of patients with spontaneous pregnancies after unsuccessful treatment cycles in Turkey and Iran. The majority were below 35 years old.

relation between age, duration of infertility, and number of treatment cycles with ART discontinuation decisions.

In general, married couples love to give priority to a full family of children. In family-based culture, such as ours, infertility is considered a major public problem which may affect the spousal relationship, since there is pressure from both family and the public on infertile couples. This stressful situation becomes even more serious when the wife encounters infertility [20]. On the other hand, despite the legality of adoption in our societies, couples usually regret seeking the adoption program, mainly because they want to restore their infertility secretly. Even in Iran, where donation is legal, infertile couples prefer not using this option. It is important for them to use their own biological gametes in an ART program. Therefore it is necessary that health care professionals discuss all possible options with infertile couples in a caring, educational atmosphere.

Another investigated subject was spontaneous conception after ART failure. Many couples were found to become pregnant after ART failure. In Japan and France, spontaneous pregnancy after delivery of an IVF baby was observed in 18% and 9% of the couples, respectively [21,22]. Hennelly et al. [23] reported that 20.7% of their couples conceived spontaneously after IVF treatment and few of those who underwent ICSI also conceived. There are also reports that couples with male factor infertility had spontaneous pregnancy. In this regard, Osmanagaoglu et al. [3] reported that 11.5% of Belgian couples that discontinued ICSI treatments, conceived spontaneously. We do not know the reason for the differences between the studies, but it may be related to the differences between time intervals after ART treatment and the start of the study. The rate of spontaneous pregnancy after failed ART in Iran is close to other studies, but it was higher in cases with female factor infertility. It has been suggested that spontaneous pregnancies may be related to the ovarian stimulation given in the past, or to the physiological effects of pregnancy on the pituitary and endocrine systems [24]. The most likely cause, however, is the relief from stress [24] that undoubtedly occurs after an infertile couple finally has a child.

In conclusion, dropout rates from the ART programs are low. The majority of couples who discontinued treatment had financial problems. Therefore it becomes essential for health professionals to support infertile couples fully. Patients whose ART treatment was unsuccessful should be encouraged about other options, such as child adoption.

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