Original Article

Discontinuation Decision in Assisted Reproductive Techniques

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Abstract

Background: *In vitro* fertilization (IVF) and intra cytoplasmic sperm injection (ICSI) are recognized as established and increasingly successful forms of treatment for infertility, yet significant numbers of couples discontinue treatment without achieving a live birth. This study aims to identify major factors that influence the decision to discontinue IVF/ICSI treatments.
Materials and Methods: We studied the data of 338 couples who discontinued their infertility treatments after three cycles; based on medical records and phone contact. The main measure was the reason for stopping their treatments.
Results: Economical problems were cited by 212 couples (62.7%), as their mean income was significantly less than other couples ($p<0.0001$). Lack of success was reported as a reason by 229 (67.8%), from whom 165 (72%) also had economical problems. Achieving independent-ART pregnancy was the reason for discontinuation in 20 (5.9%) couples. Psychological stress, depression and anxiety were reported as other cessation factors by 169 (50%), 148 (43.8%) and 182 (53.8%) couples, respectively.
Conclusion: This survey suggests that the most common reasons for assisted reproductive technique (ART) discontinuation after three cycles are: prior unsuccessful cycles, economical and psychological problems. Therefore, the substantial proportion of couples could benefit from psychological intervention, increasing awareness of ART outcomes and health funding to cope more adequately with failed treatments.

Keywords: IVF, ICSI, Patient Dropout

Introduction

Couples who seek infertility treatments are considered highly motivated in achieving pregnancy. However, around 50% of those who initiate *in vitro* fertilization (IVF) will not conceive. This is partly due to the high drop out rates after an unsuccessful IVF cycle (1).

In published studies, infertility patients demonstrate a surprisingly high treatment dropout rate from fertility clinics, ranging from 23% (2) to 45% (3). A prospective cohort study of 450 Swedish couples who started IVF treatment and did not achieve a live birth reported that 54% discontinued treatment before completing the three cycles. In one study up to 25% of patients who undergone the first IVF cycle avoid further treatment and were therefore deprived of additional chances of conceiving (4).

The investigators reported that a majority of these discontinuations were due to the psychological burden of treatment (26%) or poor prognosis (25%). Other reasons for discontinuation included spontaneous pregnancy (19%), physical burden (6%) and serious disease (2%) (5). Goldfarb et al (6) reported that lack of finance was the major reason for discontinuation of treatment after a failed IVF cycle. However, another study showed a relatively high drop out rate despite the treatment being free of charge (5).

Despite advanced progress in ART treatments in Iran; the drop out rate remains high. There is no clear investigation for following up on infertile couples dropping out of the clinic, understanding the factors which influence why couples never return and their reasons for dropping out. The aim of the present study is to determine the reasons for

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discontinuation of treatment as well as the relationships between demographic characteristics and couples reasons for dropping out.

Materials and Methods

This investigation was a cross-sectional study. Data were collected from 376 couples who did not achieve pregnancy and discontinued treatment after completing three subsidized ART cycles (156 cases of IVF and 220 cases of ICSI cycles) between January 2005 and December 2006 at Royan Institute. Only couples with primary infertility were eligible for participation in this study.

The present study focused on couples who dropped out of the clinic that were defined as lost to follow-up which was consistent with the previous literature (7). Lost to follow-up referred to couples who failed to return to the clinic with no indication of future desire for treatment.

The data of this study were obtained from a questionnaire, which was completed by reviewing medical records or by telephoning couples whose current phone numbers were available from the unit database. Patients were contacted by telephone in a uniform manner to ascertain whether pregnancy had occurred, and if not, whether there was a reason that the couple decided not to return to the clinic. To ensure uniformity of questioning, a script was used by the individual who made the phone call in order to standardize the questions asked. The Beck and Spiel Berger questionnaire were completed by phone.

The couples who had no reliable contact numbers were excluded from participating in the study (n=38) (Fig 1).

Each patient signed a written fuly informed consent statement before inclusion in the study. They were guaranteed confidentiality and anonymity. This study was approved by the Ethics Committee at Royan Institute.

The questionnaire consisted of three parts: the first part was for demographic data (couples ages, residence, education, treatment cost and income); the second part updated the details of their assisted conception treatment (marriage duration, cause of infertility, number of previous ART attempts); and the third part determined if treatment had been discontinued and any reason for discontinuation. The follow up period was a minimum of 6 months after the third completed IVF-ICSI cycle.

The reasons for discontinuation were categorized based on: economics (social status, divorce or material problems, change of residence); psychological (depression or anxiety); medical (the couple stopped treatment as recommended by their physician due to poor prognosis, physical burden, or serious disease in one partner), and personal reasons (fear of possible ART complications, etc).

Clinical pregnancy was defined as a positive heart-

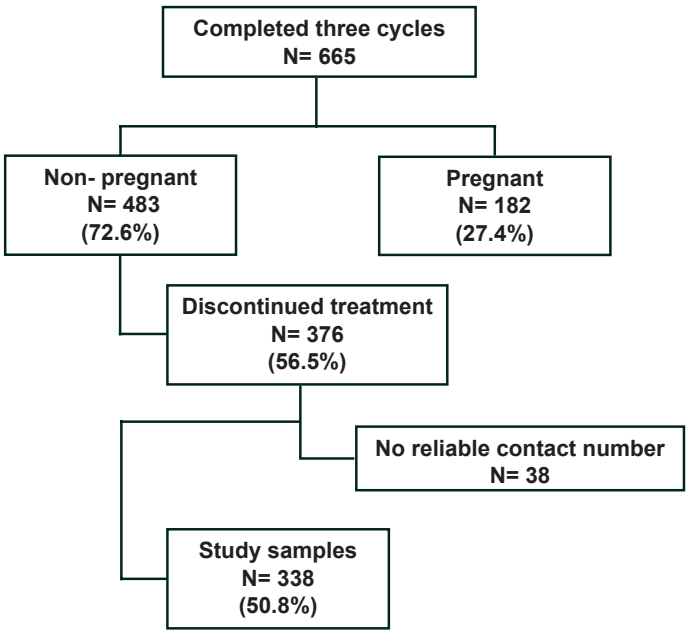

Fig 1: The outcomes of couples who completed three ART cycles between January 2005 and December 2006

beat on transvaginal ultrasound, 5 weeks after embryo transfer.

Depression was measured by means of the Beck Depression Inventory (BDI) (8); one of the most widely used, reliable, and valid instruments to assess intensity of depression and detect depression in the general population. This measure included 21 items; the scores for each item range from 0 (low) to 3 (high); and a total score range from 0 to 63. Square roots were taken of the scores to obtain a normal distribution.

Anxiety was measured by means of the State and Trait Anxiety Inventory (9), a scale with satisfactory reliability and validity. *Trait anxiety* refers to the general tendency of an individual to be anxious, whereas *state anxiety* refers to the anxiety level of an individual at a given moment. Both measures include 20 items, the score for each item ranges from 1 to 4, with higher scores indicating greater anxiety. The total scores range from 20 to 80.

Statistical Analysis

All statistical were performed by means of the SPSS program (version 13). Statistical comparison between groups was performed by chi-square test or independent sample t-test (two sided). A pvalue of <0.05 was considered significant. The data were expressed as Means ± Standard deviation. We used numbers and percentages for expression of categorical or descriptive data.

Results

Of the 2500 couples who attempted ART during 2005-2006, 376 couples discontinued subsidized treatment of their own will. These couples completed three stimulated cycles at Royan Institute. There were 38 couples who had no reliable address or contact number; therefore they were excluded from the study.

The couple's demographic characteristics are shown in Table 1. Seventy two percent of couples completing three cycles had not achieved pregnancy. The drop out rate was 56.5% for couples who had undergone three cycles. Percentages for each of the reasons suggested for discontinuing treatment in the questionnaire are shown in Table 2 in descending order. Some couples gave more than one reason for discontinuing treatment.

The most common reason for discontinuing treatment was previous unsuccessful cycles (67.8%). Economic problems (62.4%), anxiety (53.8 %), and psychological stress (50%) were the other most important factors influencing the decision to discontinue treatment.

Table 1: Demographic characteristics in couples who discontinued their treatment after three cycles

Mean (SD) age of women (year)	33.57	5.5
Mean (SD) age of partners (year)	38.1	5.6
Cause of infertility		
Male factor	100	29.6
Female factor	130	38.5%
Both	75	22.2%
Unexplained	33	9.8%
Woman education		
Primary/high school	91	27.2%
College	132	39.8%
Academic	110	32.9%
Partner education		
Primary/high school	80	24%
College	124	37.1%
Academic	110	32.9%
Mean (SD) duration of marriage	10.17	5.07
Previous IVF cycle	156	41.49%
Previous ICSI cycle	220	58.51%
Mean (SD) treatment cost ($)	27230	18930
Mean (SD) couple income ($)	5150	5905

In the present study, the correlation between drop-out reasons was also measured by chi-square test. About 78 % of couples who refused treatment because of previous unsuccessful cycles had economic problems ($p<0.0001$). The majority of women who discontinued their treatments as a result of previous unsuccessful cycles had psychological stress (54.1%), depression (91.8 %) and anxiety (65.9%) ($p<0.05$). Economic problems were observed in 86% of patients who dropped out of their treatments due to lack of suitable residency. There were significant differences between economic reasons with anxiety ($p<0.0001$), and between economic reasons with depression ($p<0.0001$). Women who had more depression or anxiety also had increased family problems ($p=0.005$, $p=0.004$, respectively).

The infertility causes were different in couples who dropped out of their treatment due to lack of successful spontaneous pregnancy ($p<0.05$). Patients who discontinued their treatments due to lack of success in previous ART cycles, because of female factor (38.1%), had the most common infertility causes. However, 40.7% of patients with a diagnosis of female infertility experienced ART independent pregnancy.

Table 2: Reasons for discontinuing of ART treatment

Reason	Number (n)	Percent (%)
Lack of success in previous treatment	229	67.8
Economic	212	62.7
Anxiety	182	53.8
Psychological stress	169	50
Depression	148	43.8
Lack of proper residency	139	41.1
Fear of possible danger	86	25.4
Couples decision	51	15.1
Familial problems	39	11.5
Physician advice	25	7.4
Repeated abortion	23	6.8
Physical buburden	22	6.5
Spontaneous pregnancy	20	5.9
Fear of genetic disorders	20	5.9
Divorce	6	1.8
Serious disease in woman	6	1.8
Serious problem in spouse	5	1.5

Discussion

Our results showed that the overall drop out rate (56.5%) in the course of three treatment cycles was similar to those reported in the literature (5, 10, 11). In the Netherlands, the drop out rate after three cycles was reported as 62.4 % (12); while in Sweden, this rate was approximately 54% (5). Rajkhowa et al (13) reported 34% of patients discontinued treatment without achieving pregnancy during a 6-year period.

Complex factors might have a role in the decision to discontinue ART. Of the several factors included in this study; four (repeated failure of ART treatments, economic problems, anxiety and psychological stress) were more relevant and emphasized.

Similar to Rajkhowa et al (13), in the present study the most common reason for cessation of treatment was lack of success in the previous cycles (67.8%). Different factors such as age, number of oocytes retrieved and number of embryos could act as prognostic factors for the success of repeated treatment cycles (10, 11). Couples need clear and comprehensive information about ART treatments and the chances of success (13). A better understanding of the individual prognosis for successful treatment of a couple may help in developing physician trust and reduce psychological stress associated with repeated IVF failures.

Our results showed that patients who dropped out of their treatments because of prior unsuccessful cycles had more psychological stress, depression or anxiety. The correlation between stress and poor outcome of fertility treatment has been reported in previous studies (14, 15). Many couples face treatment failure, which seem to be related to an increased prevalence of sub clinical anxiety and depression (16). However, other studies have failed to demonstrate a relationship between the emotional status of women and the outcome of assisted reproduction treatment (17, 18). Young et al showed a high stress level in the period between embryo transfers up to the pregnancy test. They concluded that psychological counseling during this period could have a positive effect on success rate (19).

In patients who discontinued their treatments due to lack of success in previous ART cycles; the most common infertility diagnosis was female factor (38.1%). It seemed that current treatments for female factor infertility could not overcome these patients' problems.

In the present study, economic problems were the second most important reason for dropping out (62.4%). The mean treatment cost was approximately $27, 230, but the mean income in our study was about $5,150. Insurance coverage for infertility treatment is uncommon in Iran and insurance companies consider infertility as a condition, not a disease. In addition, it is considered a cosmetic rather than medical treatment. Therefore, the costs of infertility evaluation and treatment are frequently passed directly to patients. In a recent publication from the Netherlands (12) where the cost of treatment for up to three cycles is covered by society, the drop out rate was approximately 60% after three cycles. Those investigators also concluded that economic reasons are of major importance. In our investigation, the percentage of income was significantly lower in patients with economic problems ($p<0.0001$). Besides insurance coverage and decreasing the rate of high-order multiple pregnancies by transferring fewer embryos; using advanced technologies that lessen the need for expensive and controlled ovarian hyper stimulation might result in improvement of the cost-effectiveness of ARTs.

Our investigation showed anxiety, psychological stress and depression as the third important reasons in couples who refused to continue treatment. Similar reports have also demonstrated the relationship between psychological problems and the decision for treatment termination (5, 6). In general, IVF treatment failure seems to be associated with a deterioration of emotional well being (18). Similar findings of increasing despair after

repeated unsuccessful cycles of IVF have been reported in most studies (5, 20, 21). Similarly, in a study by Verhaak et al (16), over 20% of the women who did not achieve pregnancy showed sub clinical depression and/or anxiety up to 6 months after treatment termination. Besides financial problems, different IVF procedures such as: daily injections, repeated ultrasounds and oocyte retrieval might be a cause of psychological distress in IVF treatments. In the present study, women with anxiety and depression also had economic problems ($p<0.0001$). Financial supports, good familial relationships and receiving more supports from providers of IVF treatments seem to be important factors for decreasing psychological burdens.

Despite a diagnosis of infertility, spontaneous pregnancies may still occur with rates of 7 to 21% observed in couples treated with ART (22, 23). ART independent pregnancies are more likely in younger women (23) and may vary according to the criteria used to select couples for ART and the underlying cause of infertility. However, in our study only 5.9% of couples discontinued their treatments due to spontaneous pregnancy.

Conclusion

In conclusion, this study suggests that the most common reasons for discontinuation of ART are prior unsuccessful cycles, economic and psychological problems. Health care providers involved in assisted conception treatment need to be more aware of the psychological stress associated with repeated attempts at IVF and provide strategies to improve outcome. In addition, by developing treatment strategies with less psychological complaints, the drop out rate may decrease. To minimize stress on couples regarding their future plans, both physicians and counselors must inform and educate couples about success rates of different treatment options, including the effect of the couple's background such as: diagnosis and age, time of treatment, and treatment termination. Imposition of insurance, coverage for infertility treatments and establishment of infertility centers in other regions of the country may eliminate economic problems.

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