

Dropout of Infertility Treatments Among Iranian Infertile Couples: A Cohort Study

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Abstract

Background: Many infertile couples seek Assisted Reproductive Technologies (ART) to achieve pregnancy. However, a high proportion of them dropout treatment due to different reasons. In the present study we aimed to evaluate the dropout/continuity rate of infertility treatments and related factors among Iranian couples.

Methods: The present retrospective cohort study was conducted on 380 eligible infertile women in four groups (95 people in each group) based on causes of infertility (male, female, unexplained, both) from April 2018 to March 2019 in infertility centers of Qom. The individuals had at least one unsuccessful IVF/ICSI (In Vitro Fertilization/ Intra Cytoplasmic Sperm Injection) or FET (Frozen Embryo Transfer) cycle. Participants were considered as treatment discontinuer if they did not refer to the infertility clinics at least six months after the failure of treatment. The research data were collected using medical records and telephone interviews.

Results: Incidence dropout rate of infertility treatments was 42.9%. Related factors in dropout were number of unsuccessful treatments ($P < 0.001$), age of women ($p = 0.01$), age of men ($p = 0.02$), and type of infertility (primary or secondary) ($p = 0.004$). Treatment dropout was higher in couples, who had one experience of unsuccessful treatment (60.1%), than those who had twice or more experiences (21.7%).

Conclusions: Dropout rate of infertility treatments was relatively high; and some demographic factors were associated with treatment continuation. It seems that couples, who have primary infertility and one unsuccessful infertility treatment, were at a greater risk of dropout and its consequences. This phenomenon can be due to the lack of awareness and adequate information.

Plain English Summary

Infertility is a global issue that involves many couples in the world. Due to importance of becoming parent in some cultures, many infertile couples decide to use assisted reproductive technologies to help them for having a child. Usage of these technologies is time-consuming and may be hard for patients to tolerate, because of physical, psychological, financial burden, and etc. So, many infertile couples decide to dropout infertility treatments before achieving optimal results.

Despite conducting various studies about dropout rate and its related factors/reasons around the world, there are not coherent data and factors are yet unknown especially among Iranian culture. We believe that better understanding of these issues will help politicians and health care providers to have better plans and programs to give information to infertile couples and support them to complete the course of treatments. In this study, we aimed to determine dropout rate and related factors. We followed a cohort of infertile couples during one year retrospectively. If participants had not referred to infertility centers after 6 months of treatment failure (IVF, ICSI or FET), they were placed in discontinuer group. The final results of our study showed that dropout incidence rate was 42.9%, which is relatively high and the most common related factors in treatment dropout were number of unsuccessful treatments, female participants' age in

the study, male participants' age in the study, and type of infertility (primary or secondary). So, it is obvious that, helpful interventions for infertile couples must be done on these factors.

Background

Infertility is a clinical condition, which means no clinical pregnancy after 12 months of unprotected and regular sex because of an impairment in natural capacity for reproducing as an individual or with his/her partner (1). This phenomenon interferes with the ability of having child and causes physical, financial, emotional, and sociocultural problems (2, 3) and has negative effects on psychological well-being, marital relationships, sexual relationships, and quality of life (4).

About 186 million people suffer from infertility and most of them live in developing countries (5). The prevalence of infertility is estimated at 13.2% in Iran (6). The prevalence of primary infertility is 2.5% and secondary infertility is 24% in the world (7). About 56% of these infertile couples, seek medical help for getting pregnant (8) such as Assisted Reproductive Technologies (ART) which has brought new hope for couples suffering from infertility (9). ART uses laboratory or clinical technology to gametes (human eggs or sperm) and/or embryos and its goal is reproduction (10).

Achieving a successful reproductive therapy is something that every infertile couple strives for (8). Success rates of a single cycle for assisted reproductive technologies are very different around the world. For example in a systematic review which was done in 2017, US and UK clinics had the highest rates between 2012–2013 (29% and 26% respectively), and Japan reporting the lowest (5%) (11). Therefore, many couples drop out the treatment after its failure. The high prevalence of treatment dropout is surprising and it is estimated about 30% of couples. However, this prevalence varies among different studies (12). Various studies have identified related factors in dropout, including: emotional factors, communication issues, delaying treatment, physical and psychological burden, personal problems, refusal to accept treatment, problems related to the infertility organization and clinics, marital issues, age of women, number of previous births, previous unsuccessful treatments, poor treatment prognosis, child adoption, spontaneous pregnancy, and lack of insurance coverage were among factors influencing the treatment drop out (8, 13-19). It is obvious that there are limited data about related factors in dropout and most studies have focused on the psychological and supportive factors and they have rarely investigated the importance of socio-demographic, reproductive and treatment factors. However, data of the National Family Growth Survey indicate that socio-demographic factors are also important in pursuing infertility treatments (20). To our best knowledge, there are three studies in Iran considering dropout rate of infertility treatments and related factors (21-23). It seems that the focus of these studies is more on financial factors and there is still a gap about other potential factors such as demographic and reproductive factors. The findings of present manuscript will help health care providers and policy makers to provide better services for their clients and help them to continue their treatments toward achieving pleasant results. Thus, due to the importance of infertility and treatment dropout, the present study was conducted to investigate the extent of dropout and demographic, social, economic and reproductive factors affecting the continuing treatment.

Methods

The present study was a retrospective cohort research which investigated two infertility centers in Qom, Iran (Roya Fertility Clinic & Reihaneh Fertility Center). The research samples included 380 eligible infertile women. Required number of samples from each center was determined based on the number of their clients during one year. Therefore, 100 participants were selected from Reyhaneh Center and 280 participants from Roya clinic

Inclusion criteria: 18-42-year-old infertile women according to the global definition of infertility (1); having at least an unsuccessful IVF/ICSI and FET cycle; having a medical history at the infertility center; volunteering for research; written consent; Iranian nationality (both couples); not being addicted to drugs and psychotropic drugs; and fluency in Persian.

Exclusion criteria: unwillingness to continue cooperation in the study.

The random simple sampling was performed in the study. We put the participants into 4 categories (95 per group) based on the cause of infertility (male, female, unexplained, both). They referred to infertility centers through one year (from April 2018 to March 2019). They have been followed for six months after unsuccessful ART, to determine if they were seeking further treatment. If they referred for further treatment during this six-month period, they were placed in the continuing treatment group, and if they did not return during this period, they were placed in treatment dropout group. A questionnaire was used to examine the socio-demographic and reproductive factors; and its questions were prepared based on literature review and similar articles. The questionnaire included two parts:

First, demographic, social and economic information (including age of men and women, educational level, place of residence, job of men and women, and level of income).

Second, reproductive and treatment information (including age of menarche, age of marriage, duration of marriage, first or second marriage, primary or secondary infertility, duration of infertility, number of pregnancies, number of live children, number of abortions, and ectopic pregnancies, cause of infertility, number and type of infertility treatments, number of unsuccessful infertility treatments and re-referral to continue treatment in the follow up period). The questionnaire was completed by using information from medical records and phone interview (after explaining the research purpose for patients, if they agreed). In fact, we conducted telephone interviews with infertile couples to ensure the accuracy of the information obtained from medical records. After completing data, we calculated infertility treatment continuity and dropout rates. We also identified factors influencing infertility treatment discontinuation after reviewing the data. As we mentioned above, the follow-up period for estimating the rate of treatment dropout in patients was considered for 6 months from the last unsuccessful ART treatment (Based on Moini 's et al research) (21).

Statistical analysis

Descriptive statistics, including tables of frequency, mean and standard deviation were used to express characteristics of participants; and the ANOVA and Kruskal-Wallis nonparametric test (for comparing educational level and family income level between groups) were utilized to compare groups with different causes of infertility. Chi-square test and Fisher's exact test, (when necessary), were used to compare relationship between different variables (such as age groups, educational levels of male and female participants and ...) and continuation or dropout of treatment. In all tests, the confidence level was 95% and the significance level was $\alpha=0.05$. SPSS-21 was used to analyze data.

Ethical Considerations

Written informed consent was obtained from all participants and included the name of the ethics committee of Shahroud University of Medical Sciences that approved the project and ethical ID:(Approval ID: IR.SHMU.REC.1397.235, Approval date: 2019/3/11).

Results

The present study indicated that more than half of participants (57.1%) continued their treatments after failure; and incidence dropout rate was 42.9%. In this study, there was a significant relationship between number of unsuccessful ART treatments (IVF, ICSI, and FET) with continuation of infertility treatments ($p<0.001$). but 60.1% of the participants who had one unsuccessful treatment discontinued their treatments, while only 21.7% of individuals with a history of two or more unsuccessful treatments dropped out their treatments (21.7%).

The average age of women in the study was 32.7 and the men's average age was 36.5. The ethnicity of 51.8% of women and 51.3% of men was Fars. 41.1% of women and 41.8% of men had a high school education. Almost, 86.3% of research samples were urban residents. 83.9% of women were housewives and 98.2% of them were married only once. Table 1 briefly presents some of the participants' demographic and fertility data.

Comparison of groups with different causes of infertility shows that, there was no significant difference between groups of study (female, male, unexplained, and both) in terms of demographic and socio-economic variables, including average age of women ($p = 0.5$) and men ($p= 0.63$), family income level ($p= 0.09$), women's educational level ($p= 0.67$) and men's educational level ($p= 0.16$), women's ethnicity ($p= 0.14$), men's ethnicity ($p= 0.13$), place of residence ($p= 0.74$), women's employment ($p= 0.65$), women's number of marriage ($p= 0.84$), average marriage duration ($p= 0.55$), and average age of marriage for women ($p= 0.64$). For these comparisons we mostly used Chi-square test (and Fisher exact test if applicable).

There was no significant difference between groups of studies for following variables: age of menarche ($p= 0.77$), type of infertility (primary or secondary infertility) ($p= 0.59$), average duration of infertility ($p= 0.7$), number of pregnancy ($p = 0.1$), number of abortions ($p= 0.5$), number of ectopic pregnancies ($p=$

0.2), number of children ($p = 0.46$), previous IVF cycles ($p = 0.08$); previous micro injection cycles ($p = 0.24$), previous egg donation cycles ($p = 0.28$), and previous FET cycles ($p = 0.83$) (Table 2).

For assessing association between potential factors and dropout of infertility treatment, we mostly used Chi-square test (and Fisher exact test if applicable). The following factors showed significant relationships with dropout of infertility treatment: Age of women ($p = 0.01$), age of men ($p = 0.02$), type of infertility (primary or secondary) ($p = 0.004$) (Table 3). Most women in treatment dropout group were over 35 years of age. However, the majority of men in both continuation group and dropout group were in the same range of age from 31 to 40. According to the interpretation of infertility type variable and results of the present study, the participants with primary infertility (88.9%) were more likely to continue infertility treatments. The number of unsuccessful treatments, as a factor influencing the treatment dropout, has already been explained ($P < 0.001$).

However, results of the present study failed to show a significant relationship between the following factors and the continuation of infertility treatments: women's education ($p = 0.13$), men's education ($p = 0.48$), men's ethnicity ($p = 0.12$), women's ethnicity ($p = 0.37$), place of residence ($p = 0.66$), economic status ($p = 0.27$), marriage duration ($p = 0.2$), marriage age ($p = 0.87$), number of pregnancy ($p = 0.11$), and number of abortions ($p = 0.055$). In addition, there was no association between the cause of infertility and continued treatment in the present study ($p = 0.19$). However, this difference was not statistically significant, most participants, who continued treatment were in unexplained cause of infertility group (63.2%) and group with a female cause (56.8%). In the treatment dropout group, most participants were in the infertility group with a male cause (51.6%) (Table 3).

Discussion

The present study aimed to determine related factors in dropout of infertility treatments and its incidence rate, so a retrospective cohort study was conducted on couples who visited the infertility centers within a year. According to results of our research dropout rate was 42.9% and most participants, who dropped out the treatment, were infertile couples with one history of unsuccessful ART treatments. This result may be due to the lack of information about assisted reproductive techniques and their success rates among this population. Different studies of various regions in the world reported a range of 5.6% (13, 24, 25) to 70% (19, 26-28) for dropout and results of the present research were consistent with results of three studies in Iran in terms of treatment dropout rate (Moini et al: 56.5%, Hossein Rashidi et al: 53.2% and Khalili et al: 28.3%) (21-23).

Many studies have provided different definitions for treatment dropout, but some studies have not presented any definitions. In the present study, our definition for dropout was failure to seek further treatments during a six-month period following at least one unsuccessful ART (IVF, ICSI, FET) cycle; and an unsuccessful treatment meant failure to achieve clinical pregnancy (to observe fetal heart rate at six weeks of pregnancy or positive pregnancy test results), or loss of pregnancy after the abortion. We did not examine dropout rate in couples being treated with IUI, because this technique was inapplicable in

cases of infertility with male or both causes, and it is applicable in infertility with female or unexplained causes and ART does not include assisted insemination (IUI) (1).

Soullier et al. conducted a prospective study on a large population (3037). They showed a 50% dropout rate was 50% after the first unsuccessful IVF cycle, 32% and 18% after second and third unsuccessful cycles respectively. Their results were consistent with the present research because in our research, dropout rate was 60.1% after the first unsuccessful treatment cycle, 10.9% and 10.8% after the second and third cycles respectively in the present study (29).

Despite more than 20 years of research on the infertility treatment dropout, most studies have not investigated the factors affecting the treatment dropout (less than 60% of studies have considered it) (8). However, a number of complex factors are involved in dropout (8, 13-19). We searched various databases to find similar studies examining the roles of demographic and fertility factors in dropping out or continuing infertility treatments, but we could find few related studies in recent years. We discuss about the results of some of them in the following paragraphs.

As previously said, we found association between women's age and treatment dropout. This finding is consistent with studies done by Gameiro et al.(8), Soullier et al. (29) and Dodge et al (30) which found women's age as a predictor of the treatment dropout. On the contrary, De Vries et al. could not show any association between women's age and treatment dropout (31).

We also could not find any relationship between women's education ($p=0.13$), cause of infertility ($p= 0.19$) and dropout While Pedro et al. could show association between women's education and type of ART techniques (couples under IVF, ICSI or TESE were likely to drop out the treatment than those undergoing drug treatment or IUI), and female cause of infertility (12). We did not assess psychological factors and it was one limitation for our study, while in a study by Pedro et al. and some other studies such as a study by Eisenberg et al., psychological factors were also examined in continuation or dropout of treatment (12, 25).

Eisenberg et al could show relationship between age (consistent with results of the present study) and economic status (inconsistent with results of the present study) with treatment dropout. However, the researchers also had different definitions for dropout from the present study; and they put individuals in the treatment dropout group if they refused to undergo the infertility tests or treatment after the primary examination by an endocrinologist. Despite the wide range of definition for treatment dropout in Eisenberg's research, the dropout rate in that study was much lower than the present study (13% vs. 42.9%) (25).

Other studies reported other reasons in dropout for instance a study done by Vassard et al. placed effective factors in two categories: 1) reasons from women's perspectives including low levels of family support, especially about infertility, conflict with friends, frequent conflicts with spouse 2) reasons from men's perspectives including overall family support, and problems in communicating with spouse about the infertility (32). A study by Moini et al., which was previously reviewed, investigated the psychological

issues and reported that a history of failed cycles, economic issues, psychological stress, depression, and anxiety were among the factors associated with the treatment dropout. They also reported that individuals with infertility with a female cause mostly drop out the treatment (21). We did not find any statistically significant association between cause of infertility and treatment continuation or dropout, but as mentioned earlier, most individuals who continued treatment in the present study (63.2%) were in the infertility group with an unexplained cause of infertility, and then those in infertility group with a female cause (56.8%). In the treatment dropout group, the majority of individuals, who dropped out the treatment, were in the male infertility group (51.6%) and it was inconsistent with a study by Vassard et al.(32).

The other limitation of present study was that the research data were collected quantitatively through a structured questionnaire, and there was no qualitative interview for deeper exploration of causes of treatment dropout. It seems that despite many studies on the infertility treatment dropout, there is a lack of qualitative study with in-depth and structured interviews, especially in Iran to find effective factors in this issue.

Conclusion

The infertility treatment dropout is very common and it seems that some demographic and fertility factors are associated with continuation of infertility treatments. In the present study, women's age of over 35 was a factor associated with the treatment dropout probably due to the weaker prognosis of the patients than younger women. However, examining whether the individuals voluntarily or on the advice of a physician drop out the treatment requires qualitative studies and data collection through in-depth interviews.

According to results of the present study, it seemed that couples, who had the history of one unsuccessful infertility treatment, are at a greater risk for dropout and its consequences, probably due to lack of awareness and sufficient information. On the other hand, couples who try to continue treatment more than once, were more likely to learn about alternative therapies and solutions, and once they failed, they were not disappointed to continue treatment. Therefore, it seems that counseling and guiding infertile couples are very important. Unfortunately, in many infertility treatments centers, counseling is ignored and midwives and psychologists are not used for providing accurate information for patients, counseling services and psychological support. Furthermore, it seems that there are few interventional studies on the continuation of treatment by couples in the world; hence, it is necessary to design extensive studies with supportive, educational, financial and other interventions to prevent dropout and its consequences, such as divorce, isolation, and the severance of social relations. In the present study, type of infertility was associated with dropout; and most individuals, who dropped out the treatment, had primary infertility. The reason why they often dropped out the treatment, needed further studies, but by experience, we found that individuals with primary infertility had less knowledge about infertility issues and treatments; and many of them were afraid of seeking advice from others because of infertility stigma, thus they gave up treatment for fear of being seen in infertility centers. As mentioned above, comprehensive studies should

be conducted on this field; and the involvement of financial factors, women's older age, and reduction of ovarian reserve and response to stimulation, etc. should not be ignored.

Abbreviations

ART: Assisted Reproductive Technology

IVF: In Vitro Fertilization

ICSI: Intra Cytoplasmic Sperm Injection

IUI: Intra Uterine Insemination

Declarations

Ethics approval and consent to participate

Written informed consent was obtained from all participants and included the name of the ethics committee of Shahroud University of Medical Sciences that approved the project and ethical ID:(Approval ID: IR.SHMU.REC.1397.235, Approval date: 2019/3/11).

Consent for publication

Not applicable.

Availability of Data and Materials

All data generated or analyzed during this study are included in this published article.

Competing Interests

Authors declare that they have no conflict of interest.

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Author's Contribution

M.G., A.K., F.S.H., M. Y., Contributed to conception and design. M.G., Contributed to data collection, M. G, M. Y.; Contributed to statistical analysis, M.G., A.K., F.S.H., M. Y.; Contributed to interpretation of data. A.K.; was responsible for overall supervision. M. G.; Drafted the manuscript, which was revised by all authors and all of them, read and approved the final manuscript.

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Tables

Table 1. Some Demographic & Reproductive Characteristic of Infertile Couples

Variable	Value
	N=380
Women's age (Years)	32.7±5.7
Men's Age (Years)	36.5±6.3
Women's Marriage Age (Years)	24.9±5.9
Marriage Duration (Years)	7.6±4.5
Menarche Age (Years)	12.9±1.9
Infertility Duration (Years)	5.4±3.9
Women's Marriage Type (Primary)	373 (98.1%)
Infertility Type (Primary)	320 (84.2%)
Family Income level (150000000-300000000 Rial)	230 (60.5%)
Women's Educational Level (High School)	156 (41.1%)
Men's Educational Level (High School)	159 (41.8%)
Women's Ethnicity (Fars)	197 (51.8%)
Men's Ethnicity (Fars)	195(51.3%)
Employment status of women (house wife)	319 (83.9%)
Residency (City)	328 (86.3%)

Table 2. Reproductive Information of Infertile Couples with different causes of infertility

Variable	Group	F	M	B	U	p-value
		N=95	N=95	N=95	N=95	
		Number (%)	Number (%)	Number (%)	Number (%)	
Infertility Type	Primary	78(82.1%)	84(88.4%)	78(82.1%)	80(84.2%)	P=0.59
	Secondary	17(17.9%)	11(11.6%)	17(17.9%)	15(15.8%)	
Number of Pregnancy	0	67(70.5%)	74(77.9%)	64(67.4%)	65(68.4%)	P=0.1
	1	13(13.7%)	14(14.7%)	24(25.3%)	16(16.8%)	
	2 & more	15(15.8%)	7(7.4%)	7(7.4%)	14(14.7%)	
Number of Abortion	0	77(81.1%)	84(88.4%)	79(83.2%)	81(85.3%)	P=0.5
	1 & more	18(18.9%)	11(11.6%)	16(16.8%)	14(14.7%)	
Number of Live Child	0	78(82.1%)	84(88.4%)	78(82.1%)	83(87.4%)	P=0.46 ¹
	1 & more	17(17.9%)	11(11.6%)	17(17.9%)	11(11.6%)	
Previous IVF Cycle	0	88(92.6%)	82(86.3%)	91(95.8%)	89(93.7%)	P=0.08
	1 & more	7(7.4%)	13(13.7%)	4(4.2%)	6(6.3%)	
Previous ICSI Cycle	0	10(10.5%)	7(7.4%)	2(2.1%)	6(6.3%)	P=0.24
	1	61(64.2%)	70(73.7%)	71(74.7%)	63(66.3%)	
	2 & more	24(25.3%)	18(18.9%)	22(23.2%)	26(27.4%)	
Previous Egg Donation Cycle	0	91(95.8%)	95(100%)	93(97.9%)	93(97.9%)	P=0.28
	1 & more	4(4.2%)	0	2(2.1%)	2(2.1%)	
Previous FET Cycle	0	75(78.9%)	74(77.9%)	72(75.8%)	70(73.7%)	P=0.83
	1	20(21.1%)	21(22.1%)	23(24.2%)	25(26.3%)	
Continuing ART Treatment	yes	54(56.8%)	46(48.4%)	57(26.3%)	60(63.2%)	P=0.19
	No	41(43.2%)	49(51.6%)	38(40%)	35(36.8%)	

- Result Obtained From Fisher Exact Test

a<0.05 / F: Female M: male B: both U: unexplained

*: Significant

Table 3. Relation between Factors & Continuation/Discontinuation ART Treatment

variable	Group	Treatment Continuation?		p-value
		Yes	No	
		Number (%)	Number (%)	
Number of Unsuccessful Previous ART Attempts	once	99(39.9%)	149(60.1%)	P<0.001*
	Twice	90(89.1%)	11(10.9%)	
	Three times & more	28(89.2%)	3(10.8%)	
Age of women(year)	<25	19(9%)	22(13.5%)	P=0.01*
	26-30	64(29%)	30(18.5%)	
	31-35	67(31%)	42(25%)	
	>35	67(31%)	69(42.5%)	
Age of Men(year)	<30	34(15.5%)	27(16 %)	P=0.02*
	31-40	141(65%)	86(53%)	
	>40	42(19.5%)	50(31%)	
Infertility type	primary	193(88.9%)	127(78%)	P=0.004*
	secondary	24(11%)	36(22%)	

a<0.05 / F: Female M: male B: both U: unexplained

*: Significant

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [completedSTROBEcohortchecklist.docx](#)