



## CLINICAL ARTICLE

# Anxiety and depression after failure of assisted reproductive treatment among patients experiencing infertility



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## ABSTRACT

**Objective:** To investigate the impact of the number of previous infertility treatment failures on anxiety and depression. **Methods:** In a cross-sectional study, individuals (men and women, but not couples) aged at least 18 years who had a history of infertility and could read and write in Persian were enrolled at the Royan Institute, Tehran, Iran, between November 1, 2013, and February 28, 2014. Participants provided demographic and infertility information and completed the Persian version of the Hospital Anxiety and Depression Scale (HADS). **Results:** Overall, 330 patients (122 men, 208 women) were included. Mean scores on the HADS anxiety and depression subscales (HADS-A and HADS-D) were  $8.40 \pm 4.51$  and  $5.95 \pm 3.54$ , respectively. In multiple regression analysis, mean HADS-A scores were significantly higher for patients with one treatment failure ( $9.57 \pm 4.58$ ) than for those without a history of treatment ( $7.79 \pm 4.13$ ;  $P = 0.003$ ). HADS-D scores were significantly higher for patients with two failures ( $6.92 \pm 3.69$ ) than for those with no previous treatment ( $5.59 \pm 3.79$ ;  $P = 0.019$ ). **Conclusion:** Patients with infertility have increased depression and anxiety after infertility treatment failure. Counseling or treatment for these potential psychological effects should be considered after infertility treatment failure.

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## 1. Introduction

Infertility is defined as a couple's inability or failure to conceive after unprotected intercourse for 6 months (women aged  $\geq 35$  years) or 12 months (women aged  $< 35$  years) [1]. It is considered a complex problem: in addition to the causative somatic or sexual disorders, infertility has a significant negative psychological and mental impact on both men and women, including those undergoing assisted reproductive technology (ART) [2,3].

Individuals affected by infertility can report loss of self-esteem, sexual distress or stress, depression, guilt, anxiety, frustration, emotional distress, and marital problems, all of which are affected by outcomes of infertility treatment. Anxiety and depression—which are considered the most prevalent mental problems—develop owing to uncertainty regarding the cause of infertility, an indefinite treatment duration, financial worries, and pressure from friends and family [4–6]. Researchers have found that psychological problems have effects on therapeutic success; decreasing psychological distress might increase the likelihood that treatment of infertility is successful [7–10].

The treatments for infertility—whether medical monitoring or hormonal therapies—can have physical, economic, and emotional effects

on infertile individuals or couples [11]. ARTs such as in vitro fertilization (IVF) and intracytoplasmic sperm injection are complex and stressful, and can enhance an individual's or a couple's distress [6]. The decision about whether to start infertility treatments is also very difficult and can provoke anxiety. Nevertheless, negative emotions before starting ARTs might not always be detrimental for outcomes [9]. Negative emotions and stress also vary during the course of treatment procedures [12]. Previous studies have also shown that, although psychological symptoms can be somewhat resolved after fertility and pregnancy, the emotional adverse sequelae of infertility can remain for a long time [8,13]. The success or failure of infertility treatment is another important factor that can alter the burden of psychological disorders: failure of ART can exacerbate psychological problems [2,14].

There are many reports on psychological mood among infertile patients, but very few studies have investigated the impact of ART failure on psychological disorders [6]. Therefore, the aim of the present study was to examine the potential impact of the number of previous infertility treatment failures on anxiety and depression among patients experiencing infertility and undergoing ART.

## 2. Materials and methods

The present cross-sectional study enrolled infertile individuals (both men and women, but not couples) attending the Royan Institute, Tehran, Iran, a referral clinic for infertility, between November 1, 2013,

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and February 28, 2014. Eligible individuals were aged 18 years or older, had a history of infertility, and were able to read and write in Persian. All participants were married and in a heterosexual relationship, as is required by Iranian law and the Islamic Sharia for couples who are referred to the infertility clinic for ART. The study protocol was approved by the Ethics Committee of Royan Institute. All participants were informed about the aims of the study and the confidentiality of the data. Eligible individuals were also assured that acceptance or refusal to participate in the research had no influence on their treatment procedures. Written informed consent was obtained from all study participants.

Participants completed two questionnaires. The demographic and fertility information questionnaire included age (years), sex (male or female), educational levels (academic or non-academic education), duration of infertility (years), cause of infertility (male factor, female factor, both, or unknown), a history of spontaneous abortion (yes or no), and number of previous infertility treatment failures (0, 1, 2, or  $\geq 3$ ).

The Persian version of the Hospital Anxiety and Depression Scale (HADS) was used in the present study, which has been shown to have satisfactory psychometric properties [15]. The original version of the scale was published in 1983 by Zigmond et al. [16] and has been used worldwide. It is a 14-item self-report instrument composed of two subscales: anxiety (HADS-A) and depression (HADS-D). Both subscales of HADS consist of seven items which are each scored on a 4-point Likert scale, ranging from 0 to 3. Across the two subscales, eight items require reverse scoring, after which the HADS-A and HADS-D totals can be summed. The HADS-A and HADS-D scores each range from 0 to 21, with higher scores indicating a higher level of anxiety and depression, respectively. A score of 8 and greater on each HADS subscale is suggestive of a psychiatric condition. Cronbach  $\alpha$  coefficient for HADS-A and HADS-D in the study were 0.860 and 0.722, respectively.

Statistical analyses were carried out with SPSS version 16.0 (SPSS Inc, Chicago, IL, USA). Questionnaires with missing values were not considered in the analyses. Continuous variables were expressed as mean  $\pm$  SD and categorical variables as number (percentage). The relationships between individual independent variables (demographic and fertility characteristics), and dependent variables (HADS-A and HADS-D) were explored via Pearson correlation coefficient, independent samples *t* test, and one-way analysis of variance (ANOVA) followed by the Duncan post hoc test (univariate analysis). Multiple linear regression analysis (multivariate analysis) was performed with the independent variables that were significant in univariate analyses at a level of 0.10.  $P < 0.05$  was considered statistically significant in multivariate analysis.

### 3. Results

During the study period, 380 patients were invited to participate in the study. In total, 330 patients (122 men and 208 women) completed the questionnaires, yielding a response rate of 86.8%. The demographic and fertility characteristics of the participants are given in Table 1. More than half the participants had a non-academic education, were affected by male factor infertility, and had no history of abortion.

The mean HADS-A and HADS-D scores were  $8.40 \pm 4.51$  and  $5.95 \pm 3.54$ , respectively. Table 2 shows the distribution of scores falling within the HADS-A and HADS-D severity cutoffs. According to HADS-A, the prevalence of anxiety (mild, moderate, and severe) was higher in women (124 [59.6%] patients) than in men (52 [42.6%]). The proportions of women and men with depression (mild, moderate, and severe) were similar (60 [28.8%] vs 42 [34.4%]).

Age was negatively associated with anxiety, although the correlation was low in magnitude ( $r = -0.151$ ;  $P = 0.006$ ). However, there was no correlation between HADS-A score and duration of infertility ( $r = -0.008$ ,  $P = 0.886$ ). The HADS-A score was significantly higher for infertile women than for infertile men ( $P = 0.003$ ) (Table 3). Patients who had an academic education obtained significantly lower HADS-A scores than did those who had a non-academic education

**Table 1**  
Demographic and fertility characteristics (n = 330).

Characteristic	Value <sup>a</sup>
Sex	
Male	122 (37.0)
Female	208 (63.0)
Age, y	
Men	$33.9 \pm 5.3$
Women	$30.3 \pm 5.4$
Educational level	
Non-academic	204 (61.8)
Academic	126 (38.2)
Duration of infertility, y	$6.2 \pm 4.1$
Cause of infertility	
Male factor	170 (51.5)
Female factor	61 (18.5)
Both	38 (11.5)
Unknown	61 (18.5)
History of spontaneous abortion	
No	288 (87.3)
Yes	42 (12.7)
Number of previous treatment failures	
0	146 (44.2)
1	77 (23.3)
2	53 (16.1)
$\geq 3$	54 (16.4)

<sup>a</sup> Values are given as number (percentage) or mean  $\pm$  SD.

( $P = 0.011$ ) (Table 3). The HADS-A score was higher for patients with a history of abortion than for those without ( $P = 0.051$ ) (Table 3). There was no significant relationship between HADS-A score and cause of infertility ( $P = 0.294$ ), but a significant difference in HADS-A score was found among the groups in terms of the number of infertility treatment failures ( $P = 0.043$ ) (Table 3). Patients who had experienced one treatment failure had the highest HADS-A score (Fig. 1, Table 3). The Duncan post hoc test revealed that patients with one infertility treatment failure had higher anxiety scores than did patients with no failures ( $P = 0.025$ ).

All independent variables that were significant at the 0.10 level in univariate analyses were included in a multiple linear regression analysis (Table 4). According to the regression coefficients, older patients had lower levels of anxiety as compared with younger patients ( $P = 0.047$ ). Anxiety scores were higher among women than among men ( $P = 0.016$ ). Patients with academic education had lower anxiety than did those with a low education level ( $P = 0.013$ ). Additionally, patients with one treatment failure obtained significantly higher HADS-A scores than did those without a history of treatment failure ( $P = 0.003$ ).

There was no significant relationship between HADS-D and age ( $r = -0.031$ ;  $P = 0.569$ ). Duration of infertility was significantly associated with depression at the 0.10 level, but the correlation was small in magnitude ( $r = 0.097$ ;  $P = 0.079$ ). HADS-D scores did not differ by sex ( $P = 0.890$ ), cause of infertility ( $P = 0.307$ ), or history of abortion

**Table 2**  
Prevalence of anxiety and depression according to HADS.<sup>a</sup>

HADS classification (score)	Male patients (n = 122)	Female patients (n = 208)	Total (n = 330)
HADS-A			
Normal (0–7)	70 (57.4)	84 (40.4)	154 (46.7)
Mild (8–10)	23 (18.9)	51 (24.5)	74 (22.4)
Moderate (11–14)	18 (14.8)	52 (25.0)	70 (21.2)
Severe (15–21)	11 (9.0)	21 (10.1)	32 (9.7)
HADS-D			
Normal (0–7)	80 (65.6)	148 (71.2)	228 (69.1)
Mild (8–10)	30 (24.6)	40 (19.2)	70 (21.2)
Moderate (11–14)	11 (9.0)	17 (8.2)	28 (8.5)
Severe (15–21)	1 (0.8)	3 (1.4)	4 (1.2)

Abbreviations: HADS, Hospital Anxiety and Depression Scale; HADS-A, HADS subscale for anxiety; HADS-D, HADS subscale for depression.

<sup>a</sup> Values are given as number (percentage).

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