

Original Article

The Role of Psychological Distress in the Relationship between Personality Dimensions and Pregnancy Outcome of Women Undergoing Assisted Reproductive Treatment (IVF/ICSI)

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Abstract

Objective: The aim of this study was to determine the role played by psychological distress in the relation between personality dimensions and pregnancy outcome of women undergoing in vitro fertilization/Intra-Cytoplasmic Injections (IVF/ICSI) treatment.

Method: This prospective cohort study was conducted for 12 months on 154 infertile women who were receiving IVF/ICSI assisted reproductive treatment for the first time. Research instruments for measuring psychological distress included the Fertility Problem Inventory (FPI) and the Depression, Anxiety, and Stress Scale (DASS-21). One of these was completed prior to ovarian stimulation and the other during the embryo transfer stage. The temperament and Character Inventory-Revised (TCI-R 125) was employed once to assess personality dimensions prior to the ovarian stimulation stage. Independent t-test, Mann Whitney test, Repeated Measures and path analysis were performed for statistical analysis of data.

Results: The results of this study showed no significant difference between the pregnant and non-pregnant groups in personality traits (Harm avoidance and self-directness) and psychological distress (FPI and DASS scores). Repeated measures showed a significant difference in stress, anxiety, and depression levels between the two stages of ovarian stimulation and embryo transfer ($P < 0.01$). Path analysis showed no significant direct and indirect effect for harm avoidance on the pregnancy outcome when psychological distress was mediated.

Conclusion: The effect of psychological factors on IVF outcomes is more complicated than is generally assumed and more studies are mandatory to clarify the relationship between personality traits and infertility treatments.

Key words: *Assisted Reproductive Technology; Fertilization in Vitro; ICSI; Intracytoplasmic Sperm Injections; Personality; Psychological Distress*

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Infertility is one of the issues that troubles the mental health of a part of the human society. It is a stressful experience and is medically defined as the inability to conceive after one year of regular sexual contact without the use of contraception (1). Infertility is a critical period forcing stress on couples that results in psychological distress (2-4). The use of assisted reproductive treatments (ART), especially in vitro fertilization (IVF) and Intra-Cytoplasmic Injections (ICSI), has been the focus of experts' attention in the last two decades. Women undergoing IVF/ICSI treatment are often depressed and anxious due to infertility, uncertainty, and poor success of treatment methods (5-10). Distress levels in women before and during assisted reproductive treatments can be a threat to the outcome of IVF/ICSI treatments (11-15).

Some studies suggested that there is a relationship between psychological distress (measured as depression and anxiety) in infertile women before and during treatment and their reduced chance of pregnancy with IVF/ICSI fertility treatments (17, 18); although some other studies found no evidence for the effect of psychological distress on the outcomes of IVF/ICSI (19-21).

Assisted Reproductive treatment is a stressful process for patients, but emotional responses vary from person to person (16). Varieties in the emotional response to a tough stressor are supposed to be specified by multiple factors defined in "vulnerability-stress models" (17) such as coping (18, 19), personality characteristics (20, 21), stressor related cognitions (22-24) and social support (17, 25). These personality traits are deemed to be risk and protective factors for the advent of depression and anxiety (12, 17, 26, 27). Personality traits are substantial indicators of emotional responses within the course of infertility treatments, specifically when IVF treatments fail or undesirable systemic sequels happen and end results are indefinite (28).

Personality traits including neuroticism (i.e. vulnerability to stress and negative emotional reactivity) are proposed as vulnerability factors and could be predictors of mood and anxiety disorders (26). Likewise, a study found that psychoneurosis (similar to neuroticism) could significantly predict infertility stress in women who had undergone IVF treatment (28).

A large number of studies have discovered resemblances in neuroticism and harm avoidance (28). For example, Gaweda found in his study that the two dimensions of harm avoidance and self-directedness were significantly associated with depression and anxiety (29). Likewise, harm avoidance was so important that it was mentioned in Fassino's study (28) as a predictor of functional infertility. This recent systematic review also found that personality factors such as neuroticism, harm avoidance and psychoticism were identified as potential risk factors for infertility disorders (28). The aim of this prospective cohort study was to examine the role played by

psychological distress in the relation between personality dimensions and pregnancy outcome of women undergoing IVF/ICSI treatment.

Materials and Methods

The present study was a prospective cohort study, conducted at the Motazedi Infertility Center, affiliated to Kermanshah University of Medical Sciences, from October 2017 to October 2018.

In this study, the selective (targeted) sampling method was used. Samples included a number of women who were referred to the Motazedi infertility treatment center and met the inclusion criteria. According to Gourounti *et al.* (30), the sample size of each group must be at least 42 women which is estimated by 10 points in state anxiety, an alpha of 0.05, and a power of 0.80. We also assumed that 45% of women will not continue to participate in our survey. Therefore, we recruited 154 women in this study and, thus, the number of samples in this study was 154 subjects. The inclusion criteria were: having a definitive diagnosis of primary infertility, being a woman over 37 years, having no previous history of IVF/ICSI, having started the initial assisted reproductive treatment, having at least primary education, and agreeing to participate in the study. The exclusion criteria were: hormonal diseases such as thyroid hormone disorders, diabetes mellitus, adrenal insufficiency, psychiatric disorders or taking psychiatric medicine, inappropriate uterine factors (including severe endometriosis), male infertility factors (including testicular biopsy), having a history of divorce and remarriage.

Measurements

The DASS scale was developed by Lovibond (1995) to measure the severity of depression, anxiety, and stress in individuals (31). Cronbach's alpha coefficients for the depression, anxiety, and stress subscales in a normative sample of 717 participants were 0.81, 0.73 and 0.81, respectively. In the present study, the DASS-21 was used. DASS-21 evaluates depression, anxiety, and stress by 7 different terms and has been validated by Sahebi *et al.* (2005) in the Iranian population. The DASS-21 is able to detect and screen for symptoms of anxiety, depression and stress over the past week. It is a self-assessment measure on a 4-point Likert scale. The range of answers varies from "never" to "always." In the present study, the Cronbach's α of each subscale were as follows: depression (0.87), anxiety (0.84) and stress (0.86).

Fertility Problem Inventory (FPI)

This multidimensional questionnaire was originally developed by Christopher (1999) (32). The FPI is a 46-item measurement instrument examining the concerns of infertile people in five dimensions: social, sexual, relationship, childfree lifestyle, and the need for parenthood. In the work by Newton *et al.*, the internal correlation for the subscales were as follows: for social concern = 0.87, for sexual concern = 0.77, for the

relationship concern = 0.82, for rejection of childfree lifestyle = 0.80, for the need for parenthood = 0.84 and the overall stress was 0.93.

To obtain the reliability of the test, FPI was translated in Iran by Alizadeh *et al.* In 1984. They first administered the questionnaire to a sample of 30 infertile people (15 men and 15 women) in Imam Khomeini Hospital. Cronbach's alpha coefficient was 78% for social issues, 77% for sexual issues, 78% for communication issues, 75% for childless lifestyle, 84% for the need for parenthood and 91% for general stress (33).

Additionally, in the present study, Cronbach's alpha for total infertility stress was 0.85.

Temperament and Character Inventory-Revised (TCI-R)

The short form of the Temperament and Character Inventory contains 125 items. Cloninger has developed this questionnaire based on the neuro-biological model (34). Instead of focusing on personality disorders, TCI-R evaluates the main dimensions of personality. Therefore, it is a proper measure for use in non-clinical populations, as in the present study. The person can choose between "correct" and "false" based on his opinion. The scores for each item vary from 1 to 0. It assesses four dimensions of temperament (novelty seeking, harm avoidance, reward dependence, and persistence) and three dimensions of character (self-directedness, cooperativeness, and self-transcendence). The score of each subscale is calculated by adding the scores of the items of the very subscale.

Two studies in Iran are dedicated to the standardization of this questionnaire. In the first study, the test-retest method was used for obtaining the reliability coefficient of the questionnaire. The correlation coefficients between the scores obtained from the test and the retest scores of 20 subjects are as follows: innovation 96%, harm avoidance 91%, reward dependence 61%, perseverance 76%, cooperation 95%, self-leadership 85% and self-transcendence 88%. The second study was carried out on a population of 1212 people who were men and women of different ages from different areas of Tehran. In this study, the reliability coefficient of test-retest for 101 subjects was reported to be higher than 0.7. Also, the validity coefficients of the scales in 1212 people are as follows: innovation 75%, harm avoidance 72%, reward dependency 87%, perseverance 90%, cooperation 76%, self-directedness 66%, and self-transcendence 66% (35).

Procedure

Women were invited to participate in the study at the intake interview prior to their first IVF/ICSI treatment cycle. After obtaining written informed consent, participants were asked to complete the questionnaires one at the start of treatment (before the beginning of the ovarian stimulation protocol) (T1), and another at the embryo transfer stage (T2). As recommended by gynecologists, scientific evidence suggests that there should be at least three menstrual periods between

microinjection operation and embryo transfer so that the patients' body is neutralized from hormonal medications, which can improve the implantation of the fetus. Patients go to the infertility center at least 3 months after the microinjection to prepare for the embryo transfer stage.

The evaluation of patients' psychological distress was carried out using demographic questionnaires, that is, the Fertility Problem Inventory (FPI), the Depression, Anxiety, and Stress Scale (DASS-21), and Temperament and Character Inventory-Revised (TCI-R -125), at T1. Measurements of FPI and DASS scores were repeated at T2 before the embryo was transferred to the mother's body. According to the studies by Awtani and Turner *et al.* (11, 36), the level of stress is different in various stages of ART. For this reason, it is better to evaluate psychological distress in different stages of treatment.

Among the 154 patients who completed the pre-microinjection questionnaires, only 88 individuals reached the embryo transfer stage, and were therefore entered into the statistical analysis.

19 out of the 66 excluded patients did not reach the embryo transfer stage because of a long time interval between the microinjection and embryo transfer stages. 12 women had cycles cancelled prior to oocyte retrieval because of poor ovarian response. 20 women had no embryo transfer because of no viable embryos or ovarian hyperstimulation. 10 patients did not follow the treatments due to financial problems and five patients continued the rest of the treatment cycle in another medical center.

Two weeks after the embryo transfer, participants were contacted via phone calls to record the positive or negative results of the pregnancy test (Beta-HCG). Since, in this study, the criterion for the success of IVF/ICSI treatment was clinical pregnancy, we were not satisfied only with the result of the Beta-HCG test, but also followed up the Ultrasonography results (fetal heart formation) of the individuals who had positive Beta-HCG test after six to eight weeks.

Ethics

This research was approved on 18 October 2017 by the ethics committee of Tehran's university of social welfare and rehabilitation sciences with the ethics code of IR.USWR.REC.1396.180. Before patients' enrollment, the study protocol was fully explained to them and an informed consent was obtained from each participant.

Data analysis

In this study, the data were analyzed using SPSS-22. Some descriptive statistics such as frequency, mean and standard deviation were used to summarize and describe the data. Independent samples t-test and chi-square test were used to compare the demographic information of. To compare the results of the infertility stress inventory (FPI), the Depression, Anxiety, Stress Scale (DASS-21), and Temperament and Character Inventory-Revised (TCI-R) among women undergoing assisted reproductive treatment, the questionnaires were filled in two stages, one at the beginning of the treatment (before

the onset of the ovarian stimulation protocol) and the other before embryo transfer. Also the independent t-test, the Mann Whitney test and the repeated measures design were employed.

The path analysis investigated the effect of the mediating variable (FPI and DASS scores) on the relationship between harm avoidance and pregnancy outcomes. In this analysis, using the partial least square method by the smart PLS software in the parameter estimation section, we assessed the path coefficients by resampling 3000 samples with the bootstrap method.

Results

The study group included 154 women undergoing IVF/ICSI assisted reproductive treatment, of whom only 88 reached the stage of embryo transfer. 67 (76.4%) subjects did not become pregnant and 21 had a positive pregnancy test. 10 (11.4%) women with a positive pregnancy test did not become pregnant clinically, and 11 (12.5%) subjects had a clinical pregnancy (live embryo).

It is important to note that in some cases, patients neglected to answer one or two items of demographic questionnaires.

The information on demographic variables as well as fertility variables of all participants are shown in Table 1.

Table 1. Comparison of Demographic Characteristics and Fertility Variables in Non-Pregnant and Positive Pregnancy Test Groups

		Non pregnant (n = 67)	positive pregnancy test (n = 21)	P-value
		Frequency (%)	Frequency (%)	
Education	middle School degree High school diploma	18 (26.9)	6(33.3)	0.84
	High school diploma or an associate degree (Undergraduate degree)	29 (43.3)	8(44.4)	
	Bachelor’s and Master’s (Post Graduate Degrees)	20 (31.54)	4 (22.2)	
Socio economic level	Low income	25 (39.6)	11 (73.3)	0.11
	Moderate income	34 (54)	4 (26.6)	
	High income	4 (6.4)	1 (6.6)	
Occupation status	Housewife	44 (89)	7 (39)	0.001
	Employed	5 (11)	11 (61)	
History of previous Abortion	Yes	10 (19.6)	5(29.4)	0.39
	No	41 (80.4)	12 (70.5)	
Age	Mean (SD)	31.39(5.05)	Mean (SD) 30.19 (4.09)	0.32
Duration of marriage (years)		7.5 (3.67)	7.35 (3.31)	0.88
Duration of infertility (years)		6.02 (3.98)	6.15 (4.36)	0.90

The chi-square tests (χ^2) show there was no statistically significant difference in the level of education, socioeconomic status and history of previous Abortion between the two groups (non-pregnant and positive pregnancy test groups). However, the two groups had a significant difference in the occupation status ($P < 0.01$); such that 61% of the participants in the positive pregnancy test group were employed, while only 11% of non-pregnant women were employed. Also, based on independent t-test results there was no statistically significant differences in age, duration of infertility and duration of marriage between the non-pregnant and positive pregnancy test groups.

Table 2 shows the means and standard deviations of personality dimensions (harm-avoidance, self-

directedness) and psychological distress (FPI and DASS-21) in the three non-pregnant, only positive pregnancy test, and clinically pregnant groups. We merged the “only positive pregnancy test group” with the “clinically pregnant group” to increase the number of pregnant women. We then used the t-test to compare the non-pregnant group scores with the positive pregnancy test group scores. Likewise, we used the Mann-Whitney test to compare the scores of the “only positive pregnancy test group” with the scores of the “clinically pregnant group.”

Table 2. Comparison of Infertility Stress, Harm-Avoidance, Self-Directedness, Depression, Anxiety and Stress between the Non-Pregnant, Positive Pregnant Test Groups and Clinically Pregnant Women in the Two Stages of Ovarian Stimulation and Embryo Transfer

	Not pregnant (n = 67)	Positive Pregnancy Test (n = 10)	Clinical pregnancy (n = 11)	T	P-Value	Mean difference	Mann Whitney	P-Value	
	Mean (SD)	Mean (SD)	Mean (SD)						
Harm avoidance	13.25 (4)	14 (14.14)	14.20 (3.44)	-0.87	0.38	-0.92	21	1	
Self-directedness	20.23 (5.14)	22.33 (1.21)	22 (1.41)	-0.86	0.39	-1.33	14.4	0.92	
Infertility stress	Ovarian Stimulation Stage	160.14 (12.96)	170.89 (12.94)	168.14 (9.35)	-2.68	0.009	-9.9	23.5	0.39
	Embryo Transfer Stage	153.04 (37.34)	163.43 (28.27)	166.75 (30.54)	-1.16	0.24	-12.14	26	0.81
Depression	Ovarian Stimulation Stage	13.51 (5.66)	12.78 (5.76)	14.25 (5.6)	-0.71	0.48	-1.13	24	0.42
	Embryo Transfer Stage	12.31 (5.21)	12 (4.79)	13.30 (5.07)	-0.45	0.65	-0.66	22.5	0.33
Anxiety	Ovarian Stimulation Stage	12.81 (5.76)	13 (4.90)	10.75 (3.28)	1.08	0.27	1.58	24.5	0.45
	Embryo Transfer Stage	12 (4.79)	12.88 (5.6)	11.30 (3.09)	-1.43	0.15	-1.84	24.5	0.45
Stress	Ovarian Stimulation Stage	14.76 (5.30)	14.44 (6.38)	14.75 (5.30)	-0.23	0.84	-0.37	24	0.72
	Embryo Transfer Stage	13.35 (5.07)	14.50 (4.07)	14.90 (4.45)	-1.17	0.24	-1.61	16	0.09

Table 2 shows the results obtained from independent t – test for comparing scores of personality dimensions (harm-avoidance, self-directedness) and psychological distress (FPI and DASS-21) between the non-pregnant and positive pregnancy test groups in the two stages of ovarian stimulation and embryo transfer. According to table 2, it can be concluded that there was no significant difference between the non-pregnant women and women with a positive pregnancy test in terms of harm avoidance, self-directedness, depression, anxiety and stress in the stages of ovarian stimulation and embryo transfer. The two groups, however, had a significant difference in infertility stress at the ovarian stimulation stage ($P < 0.01$).

The results from the Mann Whitney test were obtained to compare the mean scores of harm-avoidances, self-directedness, infertility stress, depression, anxiety and stress between the groups of women with only a positive pregnancy test and clinically pregnant women in the two stages of ovarian stimulation and embryo transfer. These results indicated that there was no significant difference between these groups in terms of infertility stress, depression, anxiety, and stress during these two stages.

Path analysis with mediation model

The results of model indicators such as Average Variance Extracted (AVE) (infertility stress = 0.953, harm avoidance = 0.844 Depression, anxiety, stress = 0.963) and composite reliability, using path analysis in smart PLS software, demonstrate good validity. In addition, as we mentioned earlier, Cronbach’s α of each factor has a high level of reliability.

The result of path analysis indicated that harm avoidance had no direct or indirect effect (mediating role of infertility stress and depression, anxiety and stress) on pregnancy outcome (Figure 1). Although, harm-avoidance had a significant relationship with the mediating variables of infertility stress ($P = 0.005$) and depression, anxiety and stress ($P = 0.018$). Infertility stress and depression, anxiety as well as stress do not demonstrate a statistically significant effect at a level less than 0.05 on the dependent variable (pregnancy outcomes).

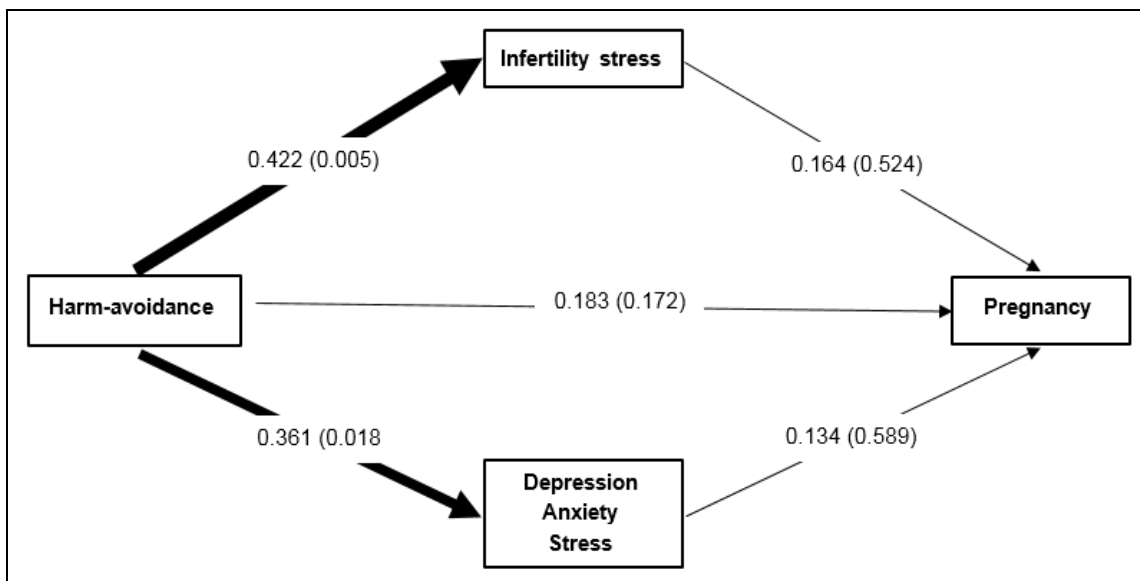


Figure 1. Conceptual Model of Relations between Harm-Avoidance, Infertility Stress, Depression, Anxiety, Stress and the Pregnancy Outcome

Research questions

Is the level of infertility stress in women undergoing assisted reproductive treatment higher during ovarian stimulation than the embryo transfer stage?

Are depression, anxiety, and stress in women undergoing assisted reproductive therapy higher during ovarian stimulation than the embryo transfer stage?

Repeated measurement test was used to answer the research questions. Repeated measurements are employed to examine whether the level of infertility stress in the ovarian stimulation phase is greater than in the embryo transfer phase. The group variable was entered as the between-group variable and the infertility stress scores of individuals in the stage of ovarian stimulation and the embryo transfer stage were considered as the within-group variable.

Before performing repeated measures analysis, Levene’s test of homogeneity of variances and Box’s M test of

equivalence of covariance matrices were performed. The results showed that Levene’s test was not statistically significant for the dependent variables and the assumption of homogeneity of variances in both stages were true.

The results of Box’s M table showed that the covariance matrices of dependent variables were the same among different groups ($P > 0.01$, Box’s $M = 2.413$).

As mentioned in the table of repeated measures (Table 3), the F value of infertility stress was not significant. Therefore, there was no significant difference between the mean scores of infertility stress in the two stages of ovarian stimulation and embryo transfer ($P > 0.01$, $F = 0.504$). Also, the interaction effect of infertility stress in the two stages of ovarian stimulation and embryo transfer was not statistically significant ($P > 0.01$, $F = 0.008$) (Table 3).

Table 3. Repeated Measures of Fertility Problem Inventory and Depression, Anxiety, and Stress Scale-21 in the Two Stages of Ovarian Stimulation and Embryo Transfer

	F	P-value	Eta
Infertility stress			
Time	0.504	0.488	0.009
Time×group	0.008	0.992	0.001
Group	0.023	0.512	0.023
Depression			
Time	69.92	0.001	0.63
Time×group	0.144	0.867	0.007
Group	0.130	0.987	0.001
Anxiety			

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Time	53.746	0.001	0.518
Time×group	0.920	0.405	0.035
Group	0.566	0.571	0.022
Stress			
Time		0.001	0.611
Time×group	1.833	0.171	0.072
Group	0.884	0.420	0.036

As the repeated measures table shows, there is a significant difference in depression between the two stages of ovarian stimulation and embryo transfer ($P < 0.01$, $F = 69.926$), so that in the embryo transfer stage, women's depression is reduced, and the results of group

comparison showed that there was no significant difference in terms of depression between the three groups of non-pregnant women, women with only a positive pregnancy test and women with a clinical pregnancy ($P > 0.01$, $F = 0.130$) (Figure 2).

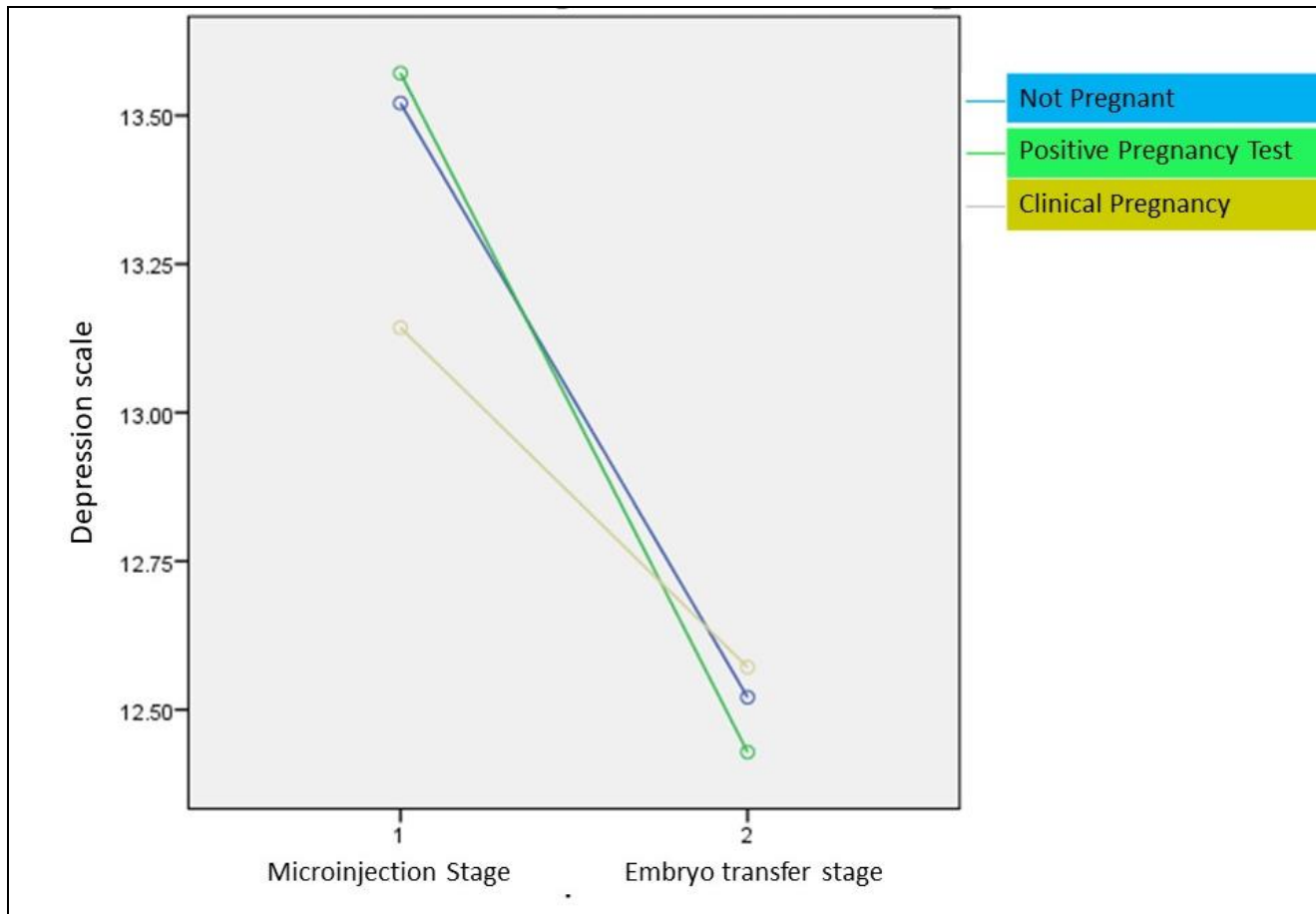


Figure 2. Comparison of the Mean Scores of Depressions between the Three Groups in the Two Stages of Depression Measurement

Results also indicated that there is a significant difference in anxiety between the two stages of ovarian stimulation and embryo transfer ($P < 0.01$, $F = 53.746$), so that in the embryo transfer stage, women's anxiety was reduced, and the results of group comparison showed that there was no significant difference in terms of anxiety between the three groups ($P > 0.01$, $F = 0.56$) (Figure 3).

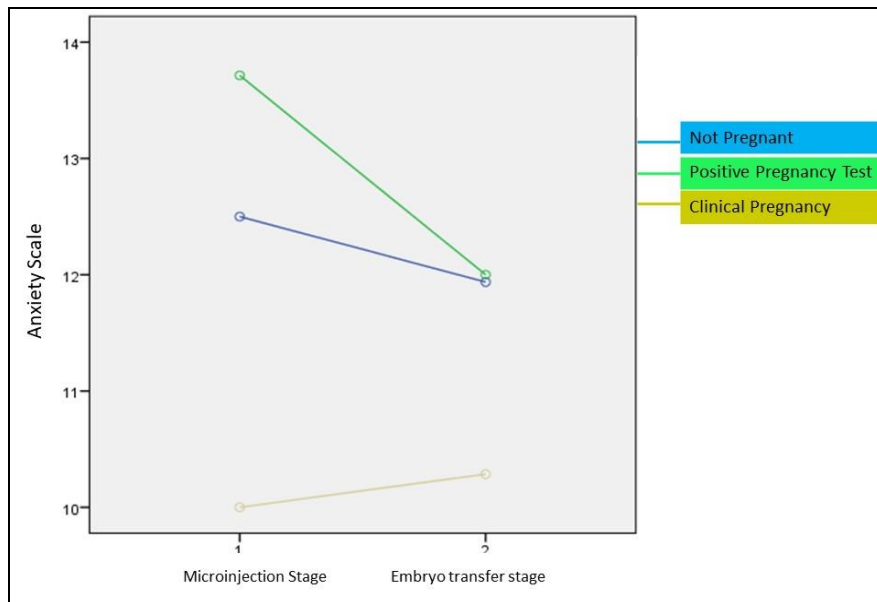


Figure 3. Comparison of the Mean Scores of Anxieties between the Three Groups in the Two Stages of Anxiety Measurement

Additionally, findings demonstrated that there is a significant difference in the level of stress between the ovarian stimulation and embryo transfer stages ($P < 0.01$, $F = 74.036$), so that in the embryo transfer stage,

women's stress was reduced, and the results of group comparison showed that there was no significant difference in term of stress between the three groups ($P > 0.01$, $F = 0.884$) (Figure 4).

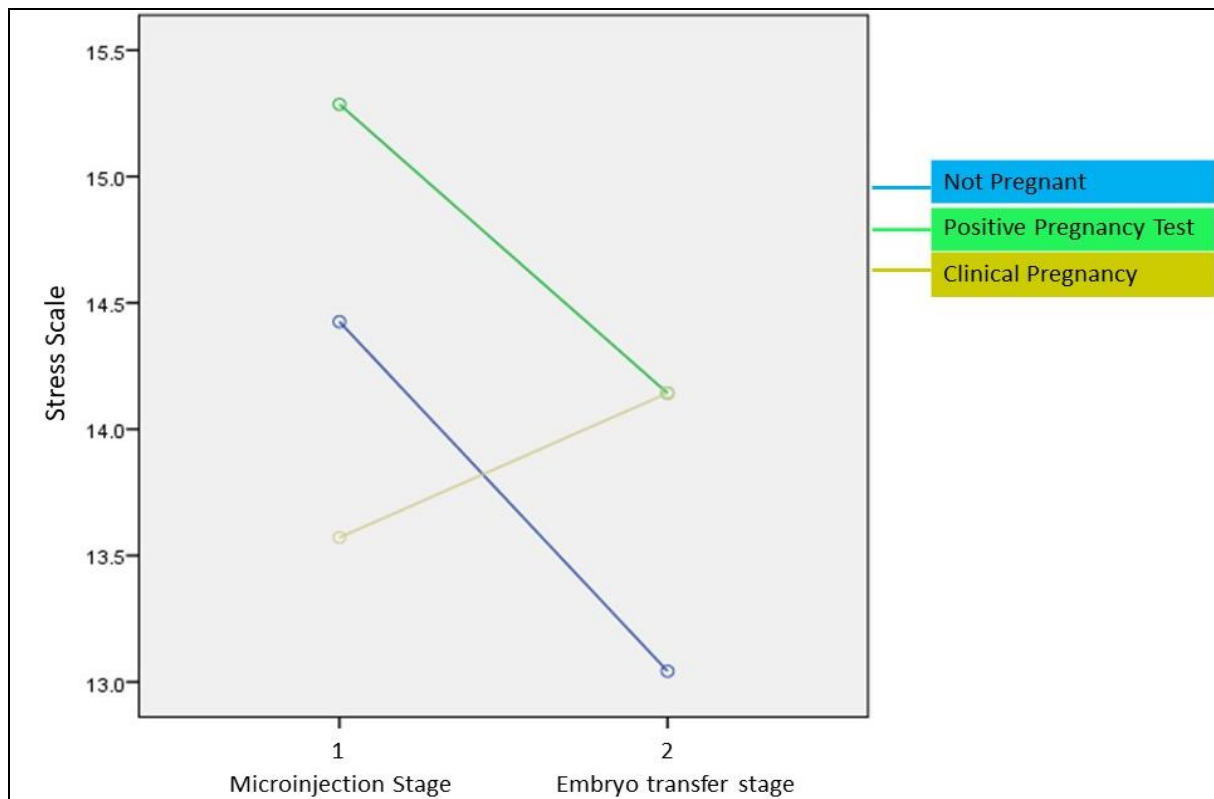


Figure 4. Comparison of the Mean Scores of Stresses between the Three Groups in the Two Stages of Stress Measurement

Discussion

The results of this study showed no significant difference between the pregnant and non-pregnant groups in Harm avoidance and self-directedness personality traits, infertility stress, and depression, anxiety and stress.

In this study we examined the hypothesis that psychological distress (FPI and DASS scores) may mediate the relationship between personality traits and pregnancy outcomes. Based on path analysis results, harm avoidance has no direct or indirect effect on the pregnancy outcome through influencing and mediating psychological distress. Also, harm-avoidance had a significant relationship with infertility stress and depression, anxiety and stress.

In a systematic review study that examined the relationship of personality factors and coping strategies with psychological distress in IVF patients, some personality factors such as Neuroticism were found to have a positive association with depression and state and trait anxiety (28). Similarly, this study mentioned the role of personality factors in predicting depression in infertile women (30). Also, Kalaitzaki *et al.* examined personality as a protective and a psychological risk factor that can be associated with the success of in vitro fertilization treatment (37). According to a systematic review and meta-analysis by Purewal, it can be noted that psychological distress may only have a relatively limited effect on the chances of pregnancy through assisted reproductive treatments. However, for some patients, this low effect can lead to a negative outcome in treatment (43).

In explaining these results, another meta-analysis (40) said that despite the persistent belief of the public (non-specialists) and some healthcare providers that anxiety reduces the likelihood of pregnancy, some scientific results (41, 45) offer accurate evidence against this belief. Given the persuading scientific path (psychological and behavioral), how can we accept these conclusions about whether distress can affect the outcome of assisted reproductive treatments? This response probably includes factors such as strategies, social support, and individual characteristics (such as optimism) that reduce the severity of distress effects.

Based on the studies by Frederiksen (46) and Turner (36), Infertile women may develop resilience through different ways to confront and treat infertility stress with the support of friends, family, and healthcare professionals, by seeking help from a psychotherapist and practicing healthy behaviors. Such factors have been shown to moderate the effects of emotional distress on other pregnancy outcomes.

Besides the reasons that exist for the inconsistency of these studies, the differences could be due to different sample sizes, differences in the tools used for measuring psychological variables, the variety of statistical methods, and pregnancy criteria (considering clinical

pregnancy with fetal heart formation at Ultrasonography or positive Beta-HCG test only).

In relation to the research question, repeated measures were used to compare the scores of FPI and DASS scores in the two stages of ovarian stimulation and embryo transfer. The results showed that there was no significant difference between infertility stress of women in the two stages of ovarian stimulation and embryo transfer. But there was a significant difference in depression, anxiety, and stress between ovarian stimulation and embryo transfer stages. Depression, anxiety and stress decrease in women during the embryo transfer phase.

In general, few studies have been conducted on the effect of psychological distress on pregnancy outcomes of ART in two stages. The research by Awtani (11) could be mentioned among the studies that have obtained results consistent with the results of this research. The results of their study showed that there was a significant difference between anxiety and stress in different stages of treatment in women under IVF / ICSI; that is on the day of ovarian stimulation (T1), on the day of embryo transfer (T2) and 10 days after embryo transfer (T3), so that the highest level of anxiety was reported 10 days after embryo transfer. Also, state anxiety was higher than trait anxiety. However, there was no significant difference between perceived stress during the three stages of treatment.

Turner *et al.* also checked stress and anxiety scores during infertility treatment in a prospective cohort study (46). Their results showed that anxiety and stress did not have significantly different scores in the three stages, that is before the start of ovarian stimulation (first stage), 1 day prior to oocyte retrieval (second stage), and five to seven days after embryo transfer (third stage). While resilience scores decrease over time, especially in patients who repeat IVF treatment, all scores before the oocyte retrieval stage (second stage) predict successful pregnancy through logistic regression. Low scores on State-Trait Anxiety Inventory (STAI) and The Perceived Stress Scale (PSS) and high scores on infertility self-efficacy (ISE) scale before ovarian recovery stage are associated with higher pregnancy rates.

On the other hand, Terzioglu *et al.* conducted a study to evaluate the effect of anxiety and depression of couples undergoing assisted reproductive treatments on pregnancy outcomes. They showed that infertile couple's depression and anxiety scores were high at the beginning of treatments and their anxiety scores decreased during the embryo transfer stage (44).

In fact, in explaining these results, it can be said that patients experience more anxiety at the beginning of the ovarian stimulation stage than before the embryo transfer stage, because poor acceptance of treatment and lack of proper knowledge about IVF is one of the main reasons for this anxiety. In addition, during the embryo transfer phase, infertile women have gone through most of the treatment stages and have become more familiar

with the hospital, doctors and medical staff, so they are more confident about the treatment, which reduces their anxiety at this stage. They experience the highest level of anxiety after the embryo transfer stage, when patients wait to know the outcome of the pregnancy.

Limitation

The limitations of the present study were the relatively large drop in subjects and the low sample size, especially in the case of pregnant women, which did not make it possible to compare the groups with the sample sizes close to each other. Additionally, the assessments made in this study were based on self-report scales, in which, despite urging the participants to provide honest answers to questions, some people may have tried to show themselves better or worse. In addition, it was not possible to evaluate the patients from the perspective of the patient's relatives. Since the research was conducted in Kermanshah, this issue should be considered in generalizing the results. Due to the limitations of the research, it is suggested that the research be done with a much higher number of samples in different regions. Moreover, evaluating the patients in the eyes of their relatives and using other tools to assess the patient accurately are highly recommended.

Conclusion

The present study has shown that the relationship between psychological factors and IVF outcomes is highly complicated and more studies are imperative to assess the complex association of several psychological factors that have direct or indirect effects on infertility treatments. An accurate, complete and up-to-date analysis of studies on the association of personality traits with the outcome of assisted reproductive treatments is essential.

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Conflict of Interest

None.

References

1. Zegers-Hochschild F, Adamson GD, de Mouzon J, Ishihara O, Mansour R, Nygren K, et al. International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) revised glossary of ART terminology, 2009. *Fertility and sterility*. 2009;92(5):1520-4.
2. Cui Y, Yu H, Meng F, Liu J, Yang F. Prospective study of pregnancy outcome between perceived

- stress and stress-related hormones. *J Obstet Gynaecol Res*. 2020;46(8):1355-63.
3. Lakatos E, Szigeti JF, Ujma PP, Sexty R, Balog P. Anxiety and depression among infertile women: a cross-sectional survey from Hungary. *BMC Womens Health*. 2017;17(1):48.
4. Aimagambetova G, Issanov A, Terzic S, Bapayeva G, Ukybassova T, Baikoshkarova S, et al. The effect of psychological distress on IVF outcomes: Reality or speculations? *PLoS One*. 2020;15(12):e0242024.
5. Litzky JF, Marsit CJ. Epigenetically regulated imprinted gene expression associated with IVF and infertility: possible influence of prenatal stress and depression. *J Assist Reprod Genet*. 2019;36(7):1299-313.
6. Miller N, Herzberger EH, Pasternak Y, Klement AH, Shavit T, Yaniv RT, et al. Does stress affect IVF outcomes? A prospective study of physiological and psychological stress in women undergoing IVF. *Reprod Biomed Online*. 2019;39(1):93-101.
7. Rooney KL, Domar AD. The relationship between stress and infertility. *Dialogues Clin Neurosci*. 2018;20(1):41-7.
8. Stanhiser J, Steiner AZ. Psychosocial Aspects of Fertility and Assisted Reproductive Technology. *Obstet Gynecol Clin North Am*. 2018;45(3):563-74.
9. Tuncay G, Yıldız S, Karaer A, Reyhani I, Özgöçer T, Ucar C, et al. Stress in couples undergoing assisted reproductive technology. *Arch Gynecol Obstet*. 2020;301(6):1561-7.
10. Zhou FJ, Cai YN, Dong YZ. Stress increases the risk of pregnancy failure in couples undergoing IVF. *Stress*. 2019;22(4):414-20.
11. Awtani M, Kapoor GK, Kaur P, Saha J, Crasta D, Banker M. Anxiety and Stress at Different Stages of Treatment in Women Undergoing In vitro Fertilization-Intracytoplasmic Sperm Injection. *J Hum Reprod Sci*. 2019;12(1):47-52.
12. Purewal S, Chapman SCE, van den Akker OBA. Depression and state anxiety scores during assisted reproductive treatment are associated with outcome: a meta-analysis. *Reprod Biomed Online*. 2018;36(6):646-57.
13. Gabnai-Nagy E, Bugán A, Bodnár B, Papp G, Nagy BE. Association between Emotional State Changes in Infertile Couples and Outcome of Fertility Treatment. *Geburtshilfe Frauenheilkd*. 2020;80(2):200-10.
14. Roussos-Ross D, Rhoton-Vlasak AS, Baker KM, Arkerson BJ, Graham G. Case-based care for pre-existing or new-onset mood disorders in patients undergoing infertility therapy. *J Assist Reprod Genet*. 2018;35(8):1371-6.
15. Stevenson EL, Trotter KJ, Bergh C, Sloane R. Pregnancy-Related Anxiety in Women Who Conceive Via In Vitro Fertilization: A Mixed Methods Approach. *J Perinat Educ*. 2016;25(3):193-200.
16. Rockliff HE, Lightman SL, Rhidian E, Buchanan H, Gordon U, Vedhara K. A systematic review of psychosocial factors associated with emotional

- adjustment in in vitro fertilization patients. *Hum Reprod Update*. 2014;20(4):594-613 .
17. Verhaak CM, Smeenk JM, Evers AW, van Minnen A, Kremer JA, Kraaijmaat FW. Predicting emotional response to unsuccessful fertility treatment: a prospective study. *J Behav Med*. 2005;28(2):181-90.
 18. Lazarus RS Folkman S. *Stress Appraisal and Coping*. New York: Springer Publishing Company; 1984
 19. Zeidner M, Endler NS, *Handbook of Coping, stress resistance, and growth: Conceptualizing adaptive functioning*. New York: Wiley 1996.
 20. Eysenck HJ. *A model for personality*. Springer Berlin Heidelberg 1981.
 21. Clark LA, Watson D, Mineka S. Temperament, personality, and the mood and anxiety disorders. *J Abnorm Psychol*. 1994;103(1):103-16.
 22. Beck AT. *Cognitive therapy of depression*: Guilford press; 1979.
 23. Alloy LB, Abramson LY, Whitehouse WG, Hogan ME, Tashman NA, Steinberg DL, et al. Depressogenic cognitive styles: predictive validity, information processing and personality characteristics, and developmental origins. *Behav Res Ther*. 1999;37(6):503-31.
 24. Abramson LY, Metalsky GI, Alloy LB. Hopelessness depression: A theory-based subtype of depression. *Psychological review*. 1989;96(2):358.
 25. Cohen S, Wills TA. Stress, social support, and the buffering hypothesis. *Psychol Bull*. 1985;98(2):310-57.
 26. Volgsten H, Ekselius L, Poromaa IS, Svanberg AS. Personality traits associated with depressive and anxiety disorders in infertile women and men undergoing in vitro fertilization treatment. *Acta Obstet Gynecol Scand*. 2010;89(1):27-34.
 27. Verhaak CM, Smeenk JM, van Minnen A, Kremer JA, Kraaijmaat FW. A longitudinal, prospective study on emotional adjustment before, during and after consecutive fertility treatment cycles. *Hum Reprod*. 2005;20(8):2253-60.
 28. Darolia S, Ghosh D. Importance of Personality Factors in Determining the Psychological Consequences of Infertility: A Systematic Review. *Health Educ Behav*. 2022;49(4):708-23.
 29. Gawęda Ł, Kokoszka A. Meta-cognitive beliefs as a mediator for the relationship between Cloninger's temperament and character dimensions and depressive and anxiety symptoms among healthy subjects. *Compr Psychiatry*. 2014;55(4):1029-37.
 30. Gourounti K, Anagnostopoulos F, Vaslamatzis G. The relation of psychological stress to pregnancy outcome among women undergoing in-vitro fertilization and intracytoplasmic sperm injection. *Women Health*. 2011;51(4):321-39.
 31. Lovibond PF, Lovibond SH. The structure of negative emotional states: comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. *Behav Res Ther*. 1995;33(3):335-43.
 32. Newton CR, Sherrard W, Glavac I. The Fertility Problem Inventory: measuring perceived infertility-related stress. *Fertil Steril*. 1999;72(1):54-62.
 33. Delavarian Z, Mohtasham N, Mosannen-Mozafari P, Pakfetrat A, Shakeri MT, Ghafoorian-Maddah R. Evaluation of the diagnostic value of a Modified Liquid-Based Cytology using OralCDx Brush in early detection of oral potentially malignant lesions and oral cancer. *Med Oral Patol Oral Cir Bucal*. 2010;15(5):e671-6.
 34. Cloninger CR, Bayon C, Svrakic DM. Measurement of temperament and character in mood disorders: a model of fundamental states as personality types. *J Affect Disord*. 1998;51(1):21-32.
 35. Kaviani H, Haghshenas H. A Preliminary Study to Standardize The Temperament and Character Inventory(Tci-125) in Persian Speakers. *Advances in Cognitive Sciences*. 2000;2(3):18-24.
 36. Turner K, Reynolds-May MF, Zitek EM, Tisdale RL, Carlisle AB, Westphal LM. Stress and anxiety scores in first and repeat IVF cycles: a pilot study. *PLoS One*. 2013;8(5):e63743.
 37. Kalaitzaki AE, Mavrogiannaki S, Makrigiannakis A. A prospective, cross-sectional study of the protective and risk psychological factors of successful in vitro fertilisation outcome: preliminary results in a Greek sample. *J Obstet Gynaecol*. 2020;40(3):382-7.
 38. Lintsen AM, Verhaak CM, Eijkemans MJ, Smeenk JM, Braat DD. Anxiety and depression have no influence on the cancellation and pregnancy rates of a first IVF or ICSI treatment. *Hum Reprod*. 2009;24(5):1092-8.
 39. Maroufizadeh S, Navid B, Omani-Samani R, Amiri P. The effects of depression, anxiety and stress symptoms on the clinical pregnancy rate in women undergoing IVF treatment. *BMC Res Notes*. 2019;12(1):256.
 40. Nicoloro-SantaBarbara J, Busso C, Moyer A, Lobel M. Just relax and you'll get pregnant? Meta-analysis examining women's emotional distress and the outcome of assisted reproductive technology. *Soc Sci Med*. 2018;213:54-62.
 41. Boivin J, Griffiths E, Venetis CA. Emotional distress in infertile women and failure of assisted reproductive technologies: meta-analysis of prospective psychosocial studies. *Bmj*. 2011;342:d223.
 42. Matthiesen SM, Frederiksen Y, Ingerslev HJ, Zachariae R. Stress, distress and outcome of assisted reproductive technology (ART): a meta-analysis. *Hum Reprod*. 2011;26(10):2763-76.
 43. Purewal S, Chapman SCE, van den Akker OBA. A systematic review and meta-analysis of psychological predictors of successful assisted reproductive technologies. *BMC Res Notes*. 2017;10(1):711.

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- 44 Terzioglu F, Turk R, Yucel C, Dilbaz S, Cinar O, Karahalil B. The effect of anxiety and depression scores of couples who underwent assisted reproductive techniques on the pregnancy outcomes. *Afr Health Sci.* 2016;16(2):441-50.
- 45 Gameiro S, Boivin J, Peronace L, Verhaak CM. Why do patients discontinue fertility treatment? A systematic review of reasons and predictors of discontinuation in fertility treatment. *Hum Reprod Update.* 2012;18(6):652-69.
- 46 Frederiksen Y, Farver-Vestergaard I, Skovgård NG, Ingerslev HJ, Zachariae R. Efficacy of psychosocial interventions for psychological and pregnancy outcomes in infertile women and men: a systematic review and meta-analysis. *BMJ Open.* 2015;5(1):e006592.