The Influence of Emotional Distress on the Outcome of In-vitro Fertilization (IVF) and/or Intracytoplasmic Sperm Injection (ICSI) Treatment among Infertile Turkish Women

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Abstract: Background: To determine whether the emotional distress of infertile Turkish women is related to social support and influences the outcome of their IVF and/or ICSI treatment. *Methods:* The Beck Depression Inventory, State-Trait Anxiety Inventory, and Social Support scales were administered to 104 primary infertile Turkish women before the date of their embryo transfer. Comparisons were made between the women who became pregnant and those who did not following the embryo transfer. *Results:* Compared to the pregnant women, the non-pregnant women had a greater number of emotional symptoms despite similar levels of social support. Also, the increased severity of depressive symptoms and higher levels of anxiety were predictive of low pregnancy rates. *Conclusion:* The pregnancy rate of infertile Turkish women was associated with emotional distress and low levels of social support were associated with increased emotional distress. Further research is needed to determine the factors and mechanisms that contribute to emotional distress in the treatment of infertility.

Introduction

Infertility is a psychological stressor and one of the most significant lifetime crises for infertile women (1–3). The stress of infertility may also stretch the limits of both coping and supporting resources of the individuals (4). Moreover, diagnostic procedures and the treatment of infertility may also influence both the physical and sexual health of the infertile women (5). As emotionally stressful situations, both the infertility itself and the treatments for it may cause depression and anxiety (1, 6, 7). On the other hand, anxiety and depressive symptoms may either be the cause or the consequence of infertility (8).

The effectiveness of infertility treatment depends on both the success rate of the treatment facility (9) and the emotional well-being of the women seeking treatment (10). Also, infertility-related stress may decrease the chances of conception but the role of anxiety and depression relative to the outcome of infertility treatment is controversial. While some studies report that increased anxiety or depression levels may result in a lower pregnancy rate (11–15), others indicate that several physiological variables, such as age, infertility duration, number of earlier failed in-vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) cycles, tubal indication for infertility, previous pregnancies, number of good quality embryos transferred and number of oocytes, are the independent predictors of infertility treatment (9, 10, 16, 17).

Whatever the nature of the interaction, the emotional effects of infertility may result from individual traits (8) and responses to infertility may depend on such attributes as adaptability, cultural expectations and social support systems (18). For example, external support from family and friends may lessen the emotional impact of infertility (4) or be an additional stressor (19). Additionally, unsupportive reactions, specific to infertility, may be associated with increased symptoms of depression and levels of overall psychological distress (20). In societies where parenthood or child bearing are of key importance, reactions to infertility can significantly shape a woman's experience with it (5, 20).

Although infertility-related anxiety and depres-

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sion are interesting areas for researchers, prior studies have mostly been from developed Western countries and cultures. Consequently, there is little knowledge about such anxiety and depression in the developing, Eastern or pronatalist countries and cultures such as Iran (12, 21), Korea (14), Taiwan (22), Turkey (11, 23–25), Japan (26), Nigeria (27), India (28, 29), Israel (30, 31), South Africa (32, 33), Egypt (34) and Kuwait (35). Studies from developing, Eastern or pronatalist countries tend to focus on society's stigmatization of infertility, (28, 29), the lack of support from husbands (11, 23, 27, 30), the association of infertility with high levels of psychological distress (21, 30–32, 35), and the importance of education and counseling about infertility and treatment approaches to infertility (33–35).

Objectives

Since relationships between family members are often very close, infertility-related problems may affect the extended family of infertile woman in developing or Eastern countries and cultures (23). Yet, only a small number of studies from those countries provide quantitative data about levels of anxiety and depression among infertile women (12, 14, 23, 24) and the impact of emotional distress on the outcome of their pregnancy (11). There is almost no related literature from those countries that addresses the relationship of social support systems to levels of depressive symptoms and anxiety among infertile women, and the effect of these conditions on the outcome of infertility treatment is not well understood. Due to a lack of research and professional counseling on this subject, we conducted a study: 1) to determine the influence of social support systems on depressive symptoms and anxiety levels among Turkish women, and 2) to investigate whether the severity of depressive symptom and anxiety levels at intake predicted the outcome of IVF and/or ICSI treatment provided to infertile women in Turkey.

Materials and Methods

Participants

The sample for this prospective longitudinal study consisted of primary infertile nulligravid married women who attended, without a referral, the Artifi-

cial Reproduction Techniques (ART) Center of Gülhane School of Medicine (a teaching hospital in Ankara, the capital of Turkey). First, the education level and income of the subjects were controlled via inclusion/exclusion criteria because of the possible effects of low education and poor income on depressive symptoms and anxiety (36, 37). In addition, it was noticed during the pilot study that women with limited education could not easily complete the psychological measures. They needed someone else's help. Since the scales represented self-report measures, it was possible that helpers may have had an impact on the results. Further, individuals with general medical conditions were excluded to control for depression and anxiety that could be associated with such medical conditions. Secondary infertile women were not included because a prior pregnancy could reduce stress associated with the treatment (38).

The quality and quantity of transferred embryos were controlled to establish a homogeneous sample. Therefore, inclusion criteria were to be married (according to Turkish laws, a necessity for ART applications), nulligravid and diagnosed as primary infertile, and to have no mood, anxiety or adjustment disorders according to DSM-IV (39). Additionally, they could be on no medications, have no medical conditions other than infertility, have a sufficient household income for the cost of ART (> $2,000 per month) and an education level of at least 11 years. Informed consent was required for all participants who completed questionnaires and provided demographic data for the study. The protocol for the study was approved by the research committee of the Department of Psychiatry, Gülhane School of Medicine.

Of the 300 consecutive infertile women who attended the ART center in a two-year period (June 2001 to July 2003), 183 refused to participate or were excluded. The reasons given by individuals who refused to participate were: transportation difficulties because of living in a rural area far from the ART center (n = 21), unwillingness to share privacy (n=19), the belief that psychiatric help was useless (n=12) and unnecessary (n=7). There were also some women who did not state a cause (n=10). Women who were excluded had a pregnancy history that terminated with or without a child (n=32), had medical conditions (diabetes, hypertension, hepati-

tis, etc.) with or without medications (n=33), had an education level less than 11 years (n=24), or had a psychiatric diagnosis (n=25). Finally, 117 married, nulligravid and primary infertile women were included in the study.

The study was designed to determine the effect of depressive symptom and anxiety levels, but not the effect of mood, anxiety or adjustment disorders on the treatment outcome of infertile women. Therefore, the SCID-I (Structured Clinical Interview for DSM-IV) (40) was used to assess those psychiatric disorders. A total of 64 women with any of those psychiatric disorders (39 with and 25 without an additional exclusion or refusal causes) were excluded.

Measurements

The Beck Depression Inventory (BDI) (41), the State-Trait Anxiety Inventory (STAI-S/T) (42), the Perceived Social Support-Family Scale (PSS-Fa) (43) and the Perceived Social Support-Friends Scale (PSS-Fr) (43) were used as standardized self-report measures.

The Turkish version of the BDI with a satisfactory validity and internal consistency (Cronbach's alpha=0.80) (44) was administered to the infertile women to rate the severity of possible depressive symptoms. The BDI is a commonly used instrument for rating the severity of depressive symptoms and is composed of 21 items that were graded between zero and three with a total score ranging from 0 to 63.

The STAI-S/T has two sections consisting of 40 items. The first 20 items measure state anxiety (STAI-S) and the second 20 items measure trait anxiety (STAI-T). A valid and reliable Turkish version with a Cronbach's alpha of 0.92 for STAI-S and 0.86 for STAI-T (45) was used in this study. Trait anxiety refers to the general tendency of an individual to be anxious. State anxiety refers to the individual's level of anxiety at a given moment. Each item has a score ranging from 1 to 4. Total scores range from 20 to 80 and higher scores indicate greater levels of anxiety.

Perceived social support from both families and friends was evaluated by a reliable and validated Turkish version of the PSS-Fa and PSS-Fr scales (Cronbach's alpha=0.88 and 0.90, respectively) (46). Each of those scales has 20 items and grade up to 40 points maximum, with higher scores indicating higher social support.

Procedure and psychiatric assessments

After an evaluation of the infertility diagnosis (primary or secondary, male or female factor, etc.) and the general medical condition, consultation-liaison psychiatrists determined whether the infertile women had any mood, anxiety or adjustment disorders using the SCID-I (40). Women included in the study were interviewed separately, so they could not influence each other. A 40 minute structured psychiatric interview was established for each subject based on the inclusion criteria. After an extended protocol, followed by gynecologists, a maximum of two embryos were transferred to each woman in the cycle. The measurements of depression, anxiety and social support were assessed for each woman on the day before her transfer date. An aim was to determine the influence of emotional distress of infertile woman on the pregnancy rate of her first treatment cycle. Repeated trials in different cycles were not taken into account and the study on each woman was terminated at the end of her first treatment cycle whether a pregnancy was obtained or not. For the women who became pregnant, the ongoing pregnancy was the end point of the investigation. For each woman, this point was determined by both β-hCG levels in the blood test 15 days after the embryo transfer date and a positive ultrasonographic finding at 7 weeks of pregnancy.

Analysis

All data analyses were performed by means of the Statistical Package for Social Sciences (Version 11.0). Frequencies were analyzed for the following variables: infertility duration, age, number of transferred embryos, and the scores on the rating scales (BDI, STAI-S/T and PSS-Fa/Fr). Differences in the data between the women who became pregnant and those who did not were analyzed using the Student's t-test and χ^2-test where needed. To determine the variables that predicted pregnancy, a binary logistic regression analysis was performed. To examine the contributions of depressive symptoms and anxiety, linear regression analysis was performed. The level for statistical significance was $p < 0.05$.

Results

Thirteen women with different causes for their infertility did not reach the embryo transfer stage because of poor response (n=8), ovarian hyperstimulation syndrome (n=3) and the non-availability of good quality embryos (n=2). The evaluation was done with the remaining 104 women who had the following causes for their infertility: idiopathic 21.20% (n=22), male factors 33.60% (n=35), female factors 24.00% (n=25) and both factors (a combination of male and female factors) 21.20% (n=22).

After the embryo transfer, according to the pregnancy criteria, of the 104 women, 47.11% (n=49) became pregnant (pregnant group). The remaining 52.89% (n=55) did not become pregnant (non-pregnant group). The numbers of transferred embryos were not different between the non-pregnant (1.54±0.50) and pregnant (1.39±0.49) groups (p=0.11). The descriptive data of the non-pregnant and pregnant women, regarding infertility duration, number of transferred embryos, age, and the scores on the rating scales (BDI, STAI-S, STAI-T, PSS-Fa, PSS-Fr) are presented in Table 1.

The mean infertility duration of 104 infertile women was 8.55±4.79 years and did not differ between the non-pregnant and pregnant groups (p=0.486). The age range was 19–41 years with a mean of 30.23±4.92, and the pregnant women (29.14±5.09) were significantly younger than the non-pregnant ones (31.20±4.59) (p=0.033).

There were significant differences regarding the severity of depressive symptoms and levels of state and trait anxiety between the women who became pregnant and those who did not. Although the mean depressive symptom scores of the whole sample (8.50±5.41) did not reach a level indicative of clinical depression, the non-pregnant women had significantly more severe depressive symptoms (10.55±5.49) than the pregnant group (6.21±4.34) (p=0.000).

The mean state-anxiety scores of all women were 36.88±8.37. However, the non-pregnant group (40.14±8.37) had significantly higher values than the pregnant group (33.21±7.91) (p=0.000). Infertile women had also higher trait-anxiety levels (47.11±6.19) and the scores of non-pregnant (49.46±5.74) group were significantly higher than the pregnant (44.47±5.64) (p=0.000).

The mean values of perceived social support from family and friends for the total sample were 26.06±5.09 and 30.03±6.43 respectively. The scores of both scales did not differ between the non-pregnant and pregnant women (p=0.381 for PSS-Fa and p=0.371 for PSS-Fr), but both groups perceived more social support from friends than family members (p=0.001 for each group).

Table 1. *The descriptive data of the non-pregnant and pregnant women containing the infertility duration, number of transferred embryos, age and the scores of rating scales*

	WHOLE SAMPLE n=104		NON-PREGNANT n=55		PREGNANT n=49		
	Range	Mean±SD	Range	Mean±SD	Range	Mean±SD	p
Number of embryos transferred	1–2	1.47±0.50	1–2	1.54±0.50	1–2	1.39±0.49	0.110
Infertility duration (years)	2–25	8.55±4.79	2–19	8.86±4.62	2–25	8.20±5.01	0.486
Age (years)	19–41	30.23±4.92	23–41	31.20±4.59	19–40	29.14±5.09	0.033
BDI	1–26	8.50±5.41	3–26	10.55±5.49	1–17	6.21±4.34	0.000
STAI-S	20–59	36.88±8.83	24–59	40.14±8.37	20–46	33.21±7.91	0.000
STAI-T	35–66	47.11±6.19	39–65	49.46±5.74	35–66	44.47±5.64	0.000
PSS-Fa	7–33	26.06±5.09	9–33	26.47±4.85	7–32	25.59±5.36	0.381
PSS-Fr	13–40	30.03±6.43	14–39	30.56±5.93	13–40	29.43±6.96	0.371

A stepwise linear regression analysis was performed to determine the predictors of depressive symptoms, and state and trait anxiety, where the age, infertility duration and perceived social support levels were the covariates (Table 2). Although all of the psychological scales (BDI, STAI-S and STAI-T) had significant negative correlations with both of the perceived social support scales (PSS-Fa and PSS-Fr) and no correlations with age and infertility duration, the perceived social support of friends was the only predictor for the severity of depressive symptoms, state anxiety and trait anxiety levels of the infertile women.

The study was aimed at determining the variables that related to and predicted pregnancy. Since the pregnancy had only the dichotomous result of "yes" or "no," binary logistic regression analysis in backward conditional stepwise procedure with two sets of variables was performed. The first set of variables

consisted of age, infertility duration, infertility cause and the number of embryos transferred. The second set included the psychological variables (the scores on the BDI, STAI-S and STAI-T). According to the first set of variables, only older age was correlated with poor pregnancy outcome. The infertility duration and the number of embryos transferred lacked this correlation (Table 3). The infertility cause had four different categories and was entered as a dummy variable set in the analysis. Accordingly, multiple values for it were not given in Table 3. Idiopathic infertility (p=0.531), male factor infertility (p=0.946), female factor infertility (p=0.629) and combined factor infertility (p=0.432) did not correlate with pregnancy outcome. Age, depressive symptoms, state and trait anxiety levels were all significant but negatively correlated with pregnancy. The severity of depressive symptoms and trait anxiety levels were the predictors of pregnancy outcomes (Table 4).

Table 2. *The linear regression model for whole sample with psychological variables and social support scores*

Dependent Variable	Model	MODEL SUMMARY				COEFFICIENT (Predictor)			
		Adjusted R^2	F	df1	p	Independent Variable	Beta	t	p
BDI	1	0.071	7.849	1	0.006	PSS-Fr	-0.267	-2.802	0.006
STAI-S	1	0.041	4.380	1	0.039	PSS-Fr	-0.203	-2.093	0.039
STAI-T	1	0.031	4.309	1	0.040	PSS-Fr	-0.201	-2.076	0.040

Table 3. *The binary logistic regression model for pregnancy as dependent variable where age, infertility duration and the number of embryos transferred were independent variables of first set*

	B	Wald Statistics	p	Odds Ratio	95,0% CI	
					Lower	Upper
Infertility duration	-0.044	0.612	0.434	1.045	0.935	1.169
Number of embryos transferred	-0.551	1.819	0.177	0.577	0.259	1.283
Age	-0.089	4.428	0.035	0.915	0.842	0.994
Constant	2.565	3.973	0.046	13.004		

Table 4. *The binary logistic regression model for pregnancy as dependent variable where age and psychological variables were independent variables*

| | B | Wald Statistics | p | Odds Ratio | 95,0% CI | |
					Lower	Upper
Age	-0.042	0.736	0.391	0.959	0.871	1.056
STAI-S	-0.049	1.907	0.167	0.952	0.888	1.021
STAI-T	-0.113	5.227	0.022	0.893	0.811	0.984
BDI	-0.122	5.020	0.025	0.885	0.795	0.985
Constant	6.176	8.049	0.005	480.868		

Discussion

This report is concerned with the relationship between infertility and stress, particularly depression and anxiety, which have been extensively discussed in the literature. It was hypothesized that a greater severity of depressive symptom and high state and trait anxiety levels would be predictors of low rates of pregnancy among infertile Turkish women. It was also hypothesized that less social support would be associated with the increased severity of depressive symptom and higher levels of state and trait anxiety.

The BDI results showed that the severity of depressive symptoms in the study group did not indicate clinical depression (44) consistent with previous studies using the BDI (23–25, 47–50). However, other studies (12, 14) found higher BDI scores. Also, the state anxiety of our study group measured with STAI-S was within a normal range for the Turkish population (45) and is in accord with previous reports (13, 23, 25, 47, 51, 52). Some other studies (14, 15, 49) found that the state anxiety levels of infertile women were high. In comparison, the trait anxiety levels of the infertile women in this study were higher than in a normal population (45). This finding is congruent with some previous studies (14, 23, 49), but not all of them (13, 47, 52).

We found that non-pregnant women had a greater severity of depressive symptoms and experienced significantly higher state and trait anxiety than the pregnant women measured before the embryo transfer date. The literature reveals contradictory re-sults concerning different scores, on psychological scales applied before the embryo transfer, between the infertile women who became pregnant and those who did not. Some studies have results consistent with our findings. For example, according to intake scores, the infertile women who could not become pregnant after the IVF and/or ICSI treatment have a greater severity of depressive symptoms (11, 12, 50) and higher state (13–15) and trait anxiety (14, 49) than the women who could become pregnant. Others found no difference between the pregnant and non-pregnant women on the scales for depression (9, 13), state anxiety (16, 53) and trait anxiety (13, 47, 52).

The severity of depressive symptoms in the study group was not high and state anxiety was within a normal range because mood, anxiety or adjustment disorders were excluded, and low levels of education and household income were controlled at intake to prevent their possible negative effects on psychological well being (36). Exclusion criteria may have caused a sampling bias if the study had sought to determine the effects of psychiatric disorders on the treatment outcome of infertile women instead of the effects of depressive and anxiety symptoms. In addition to the exclusion of infertile women with psychiatric diagnoses, the state anxiety level of the sample was low because the term "state anxiety" refers to the anxiety of an individual at a given moment and the contradictory results in the literature concerning the state anxiety levels of infertile women may arise from

the application time of the scale such as at the beginning of the investigation, during the protocol, before or after the oocyte retrieval, before the embryo transfer, etc.

The trait anxiety level of the sample was found to be higher than in the normal Turkish population in spite of anxiety and adjustment disorders which were excluded at the beginning of the study. Experiencing high trait anxiety may have been the emotional response to help seeking behavior for infertility itself and the treatment of infertility because both of those situations are indefinite, uncertain and harmful states that could make one anxious (5). Furthermore, the gender role socialization of a woman in terms of motherhood and childbearing may cause her to perceive infertility as a threat (19, 23). She may also feel more anxious because she is not fertile. Viewed differently, the magnitude of trait anxiety may be because of a general tendency of individuals to be anxious. This is well described by STAI-T and the individual trait may result in obtaining different findings from different studies. On the other hand, higher levels of trait anxiety with depressive symptoms not indicating a clinical depression and state anxiety within normal range may be the symptoms of mourning peculiar to infertility (5).

The data from binary logistic regression analysis showed that older age and higher psychological variable scores have a significant relationship to poor pregnancy outcome in the IVF and/or ICSI treatment of infertile Turkish women. First, according to binary logistic regression analysis, the age of the infertile women was related to the probability of getting pregnant. This is consistent with the previous finding (17). Later, it was found that the severity of depressive symptoms and the level of trait but not state anxiety were the predictors of pregnancy. This finding is in partial agreement with Demyttenaere et al. (54), who found that depressed women had significantly lower success rates for IVF. Also, Terzioglu (25) found both anxiety and depression had negative effects on the outcome of infertility treatment. Others (9, 16, 49, 53) suggested that psychological variables had no influence on pregnancy rates. The variables contributing to emotional distress of infertile women such as low education and income level (36), and the variables that might influence the treatment outcome such as previous pregnancies and

number of good quality embryos (9, 10, 16, 17) were controlled in the present study. Also, mood, anxiety or adjustment disorders were excluded at the beginning of our study. Different findings may arise from the inclusion/exclusion criteria of the study.

In this study, infertile Turkish women perceived the social support of family and friends to be within a normal range on those scales with no differences between the pregnant and non-pregnant groups. The relationship between infertile Turkish women and the environment were previously determined as negative by Guz et al. (23). Those two results from the same culture differed because their finding (23) was related to self report whereas we used an instrument for measuring the social support. Regardless of whether the infertile women actually get or just perceive high social support, while the milieu (both family and friends) support women as vulnerable and helpless individuals who have difficulty accepting a problem like infertility, the sharing of emotions may increase social acceptance and could serve as means of coping with the challenges (46).

Linear regression analysis showed a significant negative relationship of perceived social support with depressive symptoms and anxiety levels. This finding indicates that infertile women who perceive less social support (both family and friends) have greater depressive symptoms and anxiety levels and those perceiving more social support have fewer depressive symptoms and less anxiety levels. This finding supports the result of the previous study suggesting that external support from family and friends may lessen the emotional distress of infertility (4), but conflicts with other findings that unsupportive social interactions, specific to infertility, may be significantly associated with increased depressive symptoms and greater levels of overall psychological distress (20). However, both non-pregnant and pregnant women reported that they perceived more social support from friends than family. This difference was evident in the linear regression analysis, that is, the perceived social support of friends was an indicator for each of the BDI, STAI-S and STAI-T, whereas family was not. This result is partly surprising because it is assumed that the Turkish population, having an enclosed structure, does not share infertility problems with friends but rather with family (46). The high education level of

the study group may bring out this unexpected predictor. On the other hand, the infertile women may not share their emotional distress with the family because they may perceive the family relationships and support as a threat, such as the threat of divorce because they cannot give birth to a child to enlarge the family (11, 23).

There are some limitations to this study. First, the number of women in the group was small and all of the women in the study were nulligravid, primary infertile and highly educated. On the other hand, the psychological scales were applied only before the embryo transfer date. In this respect, those findings have particular importance and cannot be generalized. Only 14.51% of all Turkish women have an education level higher than 11 years (55), and the selection of highly educated participants may be another limitation because they are not representative of the entire population. However, for the Turkish population, the validity and reliability of BDI (44) and test-retest reliability of STAI-S/T (45) were done with university students, all of whom had an education level higher than 11 years. Therefore, we think that the restriction of education level caused the sample to be homogenous.

In conclusion, this study found that Turkish women who were undergoing IVF and/or ICSI treatment had depressive symptoms not indicating clinical depression, state anxiety within a normal range and high trait anxiety. The severity of the depressive symptoms and trait anxiety levels of the infertile woman were the predictors of the outcomes of the infertility treatment. Also it was found that the emotional symptoms were influenced by the social support level of the infertile women. According to our findings, infertile women enrolling for ART or similar remedies should be evaluated by the consultation-liaison psychiatrists for levels of depressive symptoms and anxiety not only at a definite moment of the treatment procedure but also at every step of the treatment until delivery, since pregnancy rates may increase by reducing the emotional distress of infertile women. This is another difficult and indefinite situation because the counseling given in the reproduction facilities is not sufficiently used (4). Further, social support systems and cultural factors affecting the stress perception of the individual and

the mechanism of distress on pregnancy rates need to be more thoroughly investigated.

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