

Original Article

Anxiety and Stress at Different Stages of Treatment in Women Undergoing *In vitro* Fertilization–Intracytoplasmic Sperm Injection

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ABSTRACT

Aim: The aim of the present study is to evaluate the state anxiety (the present state of mind), trait anxiety (general anxiety), as well as perceived stress in women undergoing *in vitro* fertilization (IVF) treatment at three stages: T1 (on the day of start of stimulation), T2 (on the day of embryo transfer), and T3 (10 days after embryo transfer). The data at T3 level were collected telephonically. **Methodology:** The present study was carried out on 137 women undergoing IVF intracytoplasmic sperm injection cycle at four different clinics of four cities from October to April 2016. State-trait anxiety inventory (Spielberger) and perceived stress scale (Okun, *et al.*) were used as the tools. **Statistical Analysis:** The analysis was done at two levels; descriptive and inferential (analysis of variance [ANOVA], Student's *t*-test, Levene's test) using SPSS v16. **Results:** The state anxiety was higher at all the three levels than trait anxiety. The overt anxiety was highest at T3 level (mean = 45.77) followed by T1 level (mean = 44.23) and T2 level (mean = 43.04). Perceived stress was elevated at T1 level (mean = 17.93) followed by T3 level (mean = 17.28) and T2 level (mean = 16.72). The results of ANOVA showed a significant difference in anxiety among all the three levels ($P = 0.036$), but no significant difference was found for perceived stress ($P = 0.169$). *t*-test revealed that there was a significant difference between state and trait anxiety at T1, T2, and T3 levels ($P = 0.01$, $P = 0.21$, $P = 0.00$, respectively). A significant difference was only seen between the T1 and T2 levels in perceived stress ($P = 0.052$). In state anxiety, a significant difference was observed only between T2 and T3 levels ($P = 0.23$). **Conclusion:** It was observed that anxiety and stress are present in women throughout the treatment. The waiting period (T3) is the most anxious for them and their level of state anxiety is higher compared to their trait anxiety. Perceived stress is observed to be more on the day of start of stimulation followed by the waiting period.

KEYWORDS: Infertility, *in vitro* fertilization, levels of treatment, perceived stress, state anxiety, trait anxiety

INTRODUCTION

Problems related to pregnancy, childbirth, and motherhood are complex in nature in all societies, more so in patriarchal societies. Infertility is considered as a taboo and life crisis and its consequences can be devastating. The first *in vitro* baby born in 1978 gave a new hope to infertile couples.^[1]

IVF treatment can threaten one's future, self-esteem, and intimate relationships.^[2] Whenever anyone is threatened

or frightened in any way, stress and anxiety are the likely responses. Various research studies have shown that stress and anxiety faced by women undergoing infertility is more compared to men.^[3-5] For women,

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in vitro fertilization (IVF) treatment is psychologically as well as physically very demanding.

Anxiety and stress are present in females in varying degrees before, during, and after the IVF procedure. On the day when the treatment begins, women are more concerned about the number of injections they will have to take, the kind of diet they need to follow for better result, the amount of physical pain they will have to undergo, and above all the success rate of the IVF cycle.^[6] During the follow-up scans, they are worried about the progress of their treatment.^[6] On the day of ovum pick-up as well as embryo transfer, they are anxious to know about the quality and quantity of eggs and embryos, respectively.^[7] Women have reported the 2 weeks waiting period after the embryo transfer till they get their pregnancy result to be the most stressful.^[7]

A study was done by Debora Sibel *et al.* assessed the anxiety in women undergoing IVF treatment using state trait anxiety test (STAI) on 24 women undergoing IVF treatment in Brazil. The anxiety was checked at four levels; before the initiation of ovulatory agents, before egg retrieval, before embryo transfer, and on the day before the pregnancy result. The results of this study were unexpected as high baseline STAI-S and STAI-T scores were observed in all women except for two. A nonsignificant difference on SATI-S scores was seen at intervals of high anxiety during IVF which suggested that state anxiety does not change and remain elevated at all the intervals of the treatment.^[8]

Another study by Mori *et al.* in 1997 was done in Japan on 102 infertile women undergoing IVF and embryo transfer. The anxiety of the subjects was measured using two scales; state-trait anxiety scale and manifest anxiety scale. Semi-structured interviews were also conducted to know the attitudes toward the treatment. The score of strait anxiety was found to be higher compared to general Japanese population.^[9]

An article by create fertility clinics in 2015 mentioned that anxiety and stress is present in women during and after the treatment and the wait after the embryo transfer to hear the results is the most stressful part of the IVF procedure.^[10]

This is one of the very few studies looking at stress in women undergoing IVF. Moreover, we have also studied anxiety and stress at three stages in IVF treatment to help us determine the kind of support the patient requires at each stage.

METHODOLOGY

The main aim of this study was to evaluate the state as well as trait anxiety and also to measure the perceived

stress levels in women undergoing the treatment of IVF at three stages; on the day they start their treatment (T1), on the day of embryo transfer (T2) and 10 days after the embryo transfer; also known as the waiting period (T3). The following objectives were laid for this purpose:

1. To evaluate the overall anxiety in the women undergoing intracytoplasmic sperm injection at all the three stages of the treatment as well as analyze its interaction effect
2. To assess the difference between state and trait anxiety at T1, T2, and T3 levels respectively
3. To study the difference in the state anxiety at all the three stages
4. To examine the difference in the trait anxiety at all the three stages
5. To study perceived stress in women and evaluate the difference at all the three stages of treatment as well as analyze its interaction effect.

Sample selection

The data comprised of 137 women undergoing IVF cycle. The data were collected from four IVF clinics of four different cities. Approximately 250 women were approached to be a part of the study. 239 women agreed to be a part of the study but only 137 could complete it. 59 cycles resulted into a freeze all cycle, 11 cycles were cancelled, no embryo transfer happened in 14 cycles, and 18 women either gave incomplete data or did not provide the data at all three stages.

Inclusion criteria

- Couples selected were diagnosed as infertile by the gynecologist
- All couples with primary infertility undergoing their first or second IVF cycle.

Exclusion criteria

- Unwilling to participate in the study
- Unable to understand English, Hindi or the regional language of their city
- Couples with any preexisting psychopathology.

Variables

The independent variable under study was the levels of treatment (T1, T2, and T3) whereas the dependent variables were state and trait anxiety as well as perceived stress in women.

Tools used

The tool used to measure the anxiety of the sample under study was state-trait anxiety inventory. It is developed by Spielberger, 1968, 1977. The scale consists of two forms; one is to analyze the state anxiety (Form X; a temporary condition experienced in specific situations) and the other is to measure the trait anxiety (Form Y; a

general tendency to perceive situations as threatening). It has 20 statements in each part. It is a four-point Likert scale. Spielberger reported retest figures for Form X that ranged from 0.73 to 0.86 for trait scores, while state results ranged from 0.16 to 0.54. Content validity was assessed by Okun *et al.*, who noted that the STAI covered five of eight domains for generalized anxiety disorder in the DSM-IV (Diagnostic and Statistical Manual for Mental Health).^[11]

The other tool used was perceived stress scale (PSS). It measures the level of stress that the subjects perceive they have. It has total of 10 items and is a 5-point Likert scale. It is developed by Cohen *et al.* in 1988. Cohen *et al.* (1988) showed correlations with PSS and: stress measures, self-reported health and health services measures, health behavior measures, smoking status, and help-seeking behavior.^[12]

Procedure

The feasibility of the research topic was checked by conducting a pilot study on 3–4 couples from each clinic. For data collection, a rapport was first build with the women under study. Informed consent was taken by explaining them the purpose of the study. The data were collected in a quiet room of the hospital and its confidentiality was maintained for T1 and T2 stages. For T3 stage, data were collected through telephonic interview. The data was then scored using the standardized scoring pattern of the tools used.

Statistical analysis

Statistical analysis was done at two levels; descriptive (means and standard deviation [SD]) and inferential levels (analysis of variance [ANOVA], Student's *t*-test and Levene's test). SPSS version 16 (Chicago, IL, USA) was used for the analysis.

RESULTS

Descriptive analysis

The descriptive analysis revealed that overt anxiety was highest at T3 level (mean = 45.77; SD = 12.838) followed by T1 level (mean = 44.23; SD = 12.049) and the least was observed at T2 level (mean = 43.04; SD = 12.240) [Table 1].

The state anxiety was more at all the three levels; T1 (mean = 46.11; SD = 14.81), T2 (mean = 44.74; SD = 14.66), and T3 (mean = 48.88; SD = 15.21) compared to trait anxiety; T1 (mean = 42.35; mean = 8.05), T2 (mean = 41.34; SD = 8.9), and T3 (mean = 42.66; mean = 8.95). It is also seen from the calculated means that the state as well as trait anxiety was maximum at T3 level followed by T1 and T2 [Table 2].

Perceived stress was observed to be elevated at T1 level (mean = 17.93; SD = 5.19) followed by T3 level (mean = 17.28; SD = 5.64) and T2 level (mean = 16.72; SD = 5.09) [Table 3].

Inferential analysis

To study the interaction effect of overall anxiety and perceived stress at all three levels, ANOVA was carried out, and the result obtained showed that a significant difference between all the three levels as far as anxiety is concerned ($F = 3.35$; $P = 0.036$) but no significant difference was found for perceived stress ($F = 1.79$; $P = 0.169$) [Table 4].

Student's *t*-test was used to evaluate the difference between state and trait anxiety at all the three levels and it revealed that there was a significant difference between state and trait anxiety at T1 level ($t = 2.61$; $P = 0.01$), T2 level ($t = 2.31$; $P = 0.21$), and T3 level ($t = 4.12$; $P = 0.00$). The Levene's test for equality of variances too showed a significant difference at all the three levels; T1 ($F = 8.51$; $P = 0.004$), T2 ($F = 7.69$; $P = 0.006$), and T3 ($F = 5.97$; $P = 0.015$) [Table 5].

A significant difference was only seen between the T1 and T2 levels as far as perceived stress is concerned ($t = 1.95$; $P = 0.052$). The difference in perceived stress between T2 and T3 ($t = 0.87$; $P = 0.387$) as well as between T1 and T3 ($t = 0.99$; $P = 0.322$) was statistically not significant. Even Levene's test was found to be not significant [Table 6].

As far as state anxiety is concerned, there was a significant difference observed only between T2 and T3 levels ($t = 2.29$; $P = 0.23$). The Levene's test for equality of variances was found to be not significant [Table 7].

The difference between T1 and T2 ($t = 0.28$; $P = 0.781$), T2 and T3 ($t = 1.43$; $P = 0.155$), and T1 and T3 ($t = 1.11$;

Table 1: Descriptive data of anxiety scores at the three treatment levels (T1, T2, T3)

Treatment levels	n	Mean	SD	SE	95% CI for mean		Minimum	Maximum
					Lower bound	Upper bound		
T1	274	44.23	12.049	0.728	42.80	45.66	23	126
T2	274	43.04	12.240	0.739	41.58	44.50	20	107
T3	274	45.77	12.838	0.776	44.24	47.30	20	128
Total	822	44.35	12.416	0.433	43.50	45.20	20	128

*T1=On the day of stimulation, T2=On the day of embryo transfer, T3=10 days after embryo transfer, SD=Standard deviation, SE=Standard error, CI=Confidence interval

Table 2: State-trait anxiety of women under study at the three levels of *in vitro* fertilization -ICSI treatment

State-trait anxiety at levels of treatment	Levene's test for equality of variances		<i>t</i> -test for equality of means						
	<i>F</i>	Significant	<i>t</i>	df	Significant (two-tailed)	Mean difference	SEM	95% CI of the difference	
								Lower	Upper
T1 (state-trait)	8.512	0.004	2.610	272	0.010	3.75912	1.44051	0.92316	6.59509
T2 (state-trait)	7.686	0.006	2.313	272	0.021	3.39416	1.46725	0.50555	6.28277
T3 (state-trait)	5.965	0.015	4.120	272	0.000	6.21168	1.50770	3.24344	9.17992

*T1=On the day of stimulation, T2=On the day of embryo transfer, T3=10 days after embryo transfer, IVF=*In vitro* fertilization, ICSI=Intra Cytoplasmic Sperm Injection, SEM=Standard error of mean, CI=Confidence interval

Table 3: Analysis of variance of total anxiety scores of women under study at the three treatment levels

	Sum of squares	df	Mean square	<i>F</i>	Significant
Between groups	1026.599	2	513.299	3.349	0.036
Within groups	125527.588	819	153.269		
Total	126554.186	821			

Table 4: Mean and standard deviation of state and trait anxiety in women under study at the three levels of treatment

Levels of treatment	Anxiety type	<i>n</i>	Mean	SD	SEM
T1	State anxiety	137	46.1095	14.81388	1.26564
	Trait anxiety	137	42.3504	8.05185	0.68792
T2	State anxiety	137	44.7372	14.66402	1.25283
	Trait anxiety	137	41.3431	8.93888	0.76370
T3	State anxiety	137	48.8759	15.20954	1.29944
	Trait anxiety	137	42.6642	8.94943	0.76460

*T1=On the day of stimulation, T2=On the day of embryo transfer, T3=10 days after embryo transfer, SD=Standard deviation, SEM=Standard error of mean

Table 5: Mean and standard deviation of perceived stress in women under study at the three levels of treatment

Levels of treatment	<i>n</i>	Mean	SD	SEM
Perceived stress				
T1	137	17.9343	5.19078	0.44348
T2	137	16.7226	5.08708	0.43462
T3	137	17.2847	5.63986	0.48185

*T1=On the day of stimulation, T2=On the day of embryo transfer, T3=10 days after embryo transfer, SD=Standard deviation, SEM=Standard error of mean

P = 0.27) was not significant. The same was found for Levene's test for equality of variances too [Table 8].

DISCUSSION

Overall anxiety level was found to be high at all three levels of IVF treatment. At T1 level (day of start of stimulation), the patients were more anxious compared to T2 level (day of embryo transfer). The first-timers,

who have never been through an injection phase before, get fearful on the day when they have to start with injections.^[13,14] For those slightly experienced, the memories of the past and apprehension of the upcoming phase of injections boost their anxiety.^[14] T1 is the day when they are taking a step forward toward fulfillment of their long-awaited dream and IVF is the last resort for them to have a baby.^[15] At T2 level, they have gone through most of the treatment procedure, and at that time, they are more familiar with the hospital, the doctor, and the supporting staff, so they become more confident about the treatment, which reduces their level of anxiety which is not the case at the time of T3.^[16]

The change in state anxiety (a temporary condition experienced in specific situations) without any change in the trait anxiety (a general tendency to perceive situation as threatening) signifies that it was the treatment that made women more anxious. No change in the trait anxiety assured that the though the data were collected telephonically at T3 level, the accuracy of the research study was maintained as it was done without any biases or prejudices. This study revealed the overt as well as state and trait anxiety to be highest at T3 level. The period where the patient had to wait to know the pregnancy result after embryo transfer was the most difficult one for them. It makes them very anxious as there is a lot of uncertainty present. Women dream to be mothers and they are desperate to have a child, so waiting for the result is not easy for them.

The level of stress, anxiety, and anticipation rises with each stage, peaking during the waiting period.^[17] The thoughts about "what if it does not work" make them nervous not only about their own hopes and the expectations but also of their family members and friends. During the waiting period, they are even worried about the money they have invested.^[16] One of the most difficult parts for women is to think for "good" answers to tell if the treatment did not work for them.

The patients' perceived stress was found to be higher at T1 level as it was the day when they start the treatment followed by T3 level wherein they have to wait for

Table 6: T-test values of perceived stress in women under study at three levels of *in vitro* fertilization -ICSI treatment

Perceived stress at levels of treatment	Levene's test for equality of variances		t-test for equality of means						
	F	Significant	t	df	Significant (two-tailed)	Mean difference	SEM	95% CI of the difference	
								Lower	Upper
Perceived stress (T1-T2)	0.013	0.909	1.951	272	0.052	1.21168	0.62094	-0.01078	2.43414
Perceived stress (T2-T3)	1.401	0.238	-0.866	272	0.387	-0.56204	0.64890	-1.83955	0.71546
Perceived stress (T1-T3)	1.117	0.292	0.992	272	0.322	0.64964	0.65487	-0.63961	1.93888

*T1=On the day of stimulation, T2=On the day of embryo transfer, T3=10 days after embryo transfer, IVF=*In vitro* fertilization, ICSI=Intra Cytoplasmic Sperm Injection, SEM=Standard error of mean, CI=Confidence interval

Table 7: T-test values of state anxiety in women under study at three levels of *in vitro* fertilization -ICSI treatment

State anxiety at the levels of treatment	Levene's test for equality of variances		t-test for equality of means						
	F	Significant	t	df	Significant (two-tailed)	Mean difference	SEM	95% CI of the difference	
								Lower	Upper
State anxiety (T1-T2)	0.271	0.603	0.771	272	0.442	1.37226	1.78085	-2.13374	4.87826
State anxiety (T2-T3)	0.070	0.792	-2.293	272	0.023	-4.13869	1.80503	-7.69229	-0.58508
State Anxiety (T1-T3)	0.058	0.809	-1.525	272	0.128	-2.76642	1.81394	-6.33757	0.80472

*T1=On the day of stimulation, T2=On the day of embryo transfer, T3=10 days after embryo transfer, IVF=*In vitro* fertilization, ICSI=Intra Cytoplasmic Sperm Injection, SEM=Standard error of mean, CI=Confidence interval

Table 8: T-test values of trait anxiety in women under study at three levels of *in vitro* fertilization -ICSI treatment

Trait Anxiety at the levels of treatment	Levene's test for equality of variances		t-test for equality of means						
	F	Significant	t	df	Significant (two-tailed)	Mean difference	SEM	95% CI of the difference	
								Lower	Upper
Trait anxiety (T1-T2)	2.391	0.123	-0.278	272	0.781	-0.285	1.024	-2.301	1.732
Trait anxiety (T1-T3)	1.574	0.211	-1.426	272	0.155	-1.474	1.034	-3.510	0.561
Trait anxiety (T2-T3)	0.049	0.826	-1.105	272	0.270	-1.190	1.077	-3.310	0.930

*T1=On the day of stimulation, T2=On the day of embryo transfer, T3=10 days after embryo transfer, IVF=*In vitro* fertilization, ICSI=Intra Cytoplasmic Sperm Injection, SEM=Standard error of mean, CI=Confidence interval

the result. After trying all possible natural ways of pregnancy, the hope of them getting pregnant naturally like their other family and friends is now lost. They know that they will have to undergo the treatment and that they cannot do anything about it. Poor acceptance for treatment and lack of true knowledge of IVF in society are one of the main reasons for this. When enquired, getting into the treatment itself was not perceived as stressful as much as the factors that were associated with the treatment. These factors were both internal and external. These include the perception of loss of control over things, disclosure of their infertility, fear of judgments, resulting in anger and frustration, feeling of guilt and fear that they would not be able to give happiness to their husbands and their families. Women undergoing IVF treatment hold basic concerns

such as getting a negative pregnancy test, disclosure of the treatment, and their problem of infertility itself.^[5]

CONCLUSION

It can be concluded from the findings of the present study that anxiety and stress are present in women throughout the IVF procedure. They are most anxious during the waiting period and their anxiety levels (state anxiety) are higher compared to their general anxiety levels (trait anxiety). Perceived stress is observed to be more on the day of stimulation followed by the time when they have to wait for their pregnancy result.

Limitations and implications

The present study focused on women undergoing IVF for the first or second time only. The results could be

different in women undergoing repeat cycles. Other variables such as the socio economic strata, educational background, and primary or secondary infertility could also have been taken into consideration. Only questionnaire method was used for data collection; other methods such as interviews and focused group discussion could also have been included. The sample size of the study is not very large, so the results cannot be completely generalized. The other limitations are as follows: there is a lack of control group in the study and the data at T3 level is collected telephonically. This study gives an insight that proper medical and psychological counseling is required by a patient at all steps during the treatment and depending on the level of stress and anxiety tailor-made counseling sessions should be designed for them.

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Conflicts of interest

There are no conflicts of interest.

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