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Research Article

The Effects of Fertility Treatment on Depression, Anxiety, and Marital Satisfactions

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Abstract

Objectives: To evaluate anxiety, depression, and marital satisfaction of couples undergoing fertility treatment

Methods: This was a prospective study of couples presenting for fertility treatment. All couples were provided the General Anxiety Disorder 7-item scale (GAD-7), Patient Health Questionnaire-9 (PHQ-9), and Evaluation and Nurturing Relationship Issues, Communication and Happiness (ENRICH) marital satisfaction questionnaires at the initial visit and at each mid-cycle visit. Survey responses were scored using validated methods. Depression and anxiety scores were grouped by severity using published methods. Continuous variables were compared using t-tests; categorical variables were compared using chi-square or Fisher's exact tests. Change in measured anxiety and depression was measured with Jonckheere-Terpstra tests. A repeated measures regression model was used to assess change in marital satisfaction over treatment cycles.

Results: Fifty-eight couples enrolled in the study; 18 couples completed at least one treatment cycle. There was no difference in measured anxiety between sexes during any treatment cycle. There was significant increase in female anxiety between baseline and cycle 1 (p=0.0154). A higher proportion of women had mild depression than men at both baseline (p=0.024) and cycle 1 (p=0.045). Neither men nor women had a change in depression severity over treatment cycles. There was no difference in marital satisfaction by sex at any individual treatment cycle. For both sexes, there was no change in marital satisfaction over treatment cycles (p=0.858).

Conclusions: Women had an increase in anxiety on initiation of fertility treatment, but measured levels of anxiety, depression, and marital satisfaction remained stable over treatment cycles.

Keywords: Fertility Treatment; Depression; Anxiety; Marital Satisfaction

Abbreviations

Generalized Anxiety Disorder 7-Item Scale (GAD=7); Patient Health Questionnaire-9 (PHQ-9); Evaluation and Nurturing Relationship Issues, Communication and Happiness Marital Satisfaction Scale (ENRICH); Intrauterine Insemination (IUI); In Vitro Fertilization (IVF); Assisted Reproductive Therapies (ART); Frozen Embryo Transfer (FET); Intracytoplasmic Sperm Injection (ICSI)

Introduction

It has been well documented throughout the years that women and men undergoing fertility treatment experience an increased incidence of psychiatric morbidities. Anxiety and major depressive disorder are the most common of the morbidities, afflicting 23.2% and 17.0% of the studied population, respectively [1,2]. For couples undergoing fertility treatments, the source of anxiety and depression can be two-fold: the emotional hardships after unsuccessful pregnancy attempts and the financial burden that accompanies various treatments. Women can manifest these symptoms as early as seeing a negative result from a pregnancy test [3]. Furthermore, this emotional toll persists throughout the trials of fertility treatments. Traditionally, studies have measured anxiety and depression at the completion of each treatment cycle when the outcome of the treatment (positive or negative pregnancy) can significantly impact what is measured. However, there is a need for studies performed during the middle of treatment cycles rather than at the end. This timing allows measurement of the severity of anxiety and depression without the impact of final treatment outcomes. In addition, many studies lack a male component. Male partners' psychiatric wellbeing has widespread effects that go beyond the level of the individual. It is necessary to ascertain the levels of anxiety and depression within the male because they often have a pronounced effect on the females' level of anxiety and depression. Often times, a correlation of anxiety and depression between partners, or the lack thereof, can suggest marital discord. Marital satisfaction adds another dimension to anxiety and depression in fertility studies. Naturally, the tribulations of infertility and fertility treatments affect the couple as a unit and can add immense stress to couples and affect their overall mental health as well as marital satisfaction. This study aims to assess the severity of anxiety and depression in infertility patients at different stages of their treatment, their awareness of it, and how different triggers interplay to influence their overall mental health during the treatment cycles. Additionally, we aim to assess marital satisfaction and how it changes over the course of fertility treatment.

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Materials and Methods

The Institutional Review Board of the University of Oklahoma Health Sciences Center approved this prospective, longitudinal, observational study. All new patients and their partners presenting for infertility evaluation and/or treatment were offered enrollment at their initial visit while waiting to see the physician. Subjects were given validated written questionnaires including: Generalized Anxiety Disorder 7-Item Scale (GAD-7) [4,5], Patient Health Questionnaire-9 (PHQ-9) [4,6], and ENRICH (Evaluation and Nurturing Relationship Issues, Communication and Happiness) Marital Satisfaction Scale [7]. In addition, patients' charts were evaluated for self-reported anxiety and depression as well as for infertility diagnosis and treatment outcomes. The provider completed the infertility evaluation and treatment recommendations were made which was individualized for each couple. Questionnaires were then administered mid-cycle during each subsequent treatment, up to three cycles. Treatments included clomiphene citrate or letrozole for ovulation induction or augmentation in conjunction with either timed intercourse or Intrauterine Insemination (IUI) or In Vitro Fertilization (IVF). Some couples chose not to proceed with any treatment. Repeat questionnaires were then given at mid-cycle when the female subject was ready for the hCG trigger shot to simulate the luteinizing hormone surge shortly before timed intercourse, IUI, or egg retrieval. Patient information, consisting of questionnaire responses and background information, was de-identified and each couple was given a coded identification number.

Measures

The Generalized Anxiety Disorder 7-item scale (GAD-7) was used as a brief clinical measure of generalized anxiety disorder. The GAD-7 is a seven-item standardized tool that measures severity of general anxiety with increasing scores indicating increasing severity of anxiety. Scores of 5, 10, and 15 specify mild, moderate, and severe anxiety, respectively. Utilizing a cut-off value of 10 is ideal for sensitivity alone in detecting GAD, a cut-off of 8 has alternatively been found to maximize sensitivity and specificity, 77% and 82%, respectively when detecting an anxiety disorder [8]. The Patient Health Questinnaire-9 (PHQ-9) was administered to assess depression. It uses nine questions to assess the DSM-IV criteria of depression and scores each of them from 0-3: 0 "not at all", 1 "for several days", 2 "more than half of the days", and 3 "nearly every day". Increasing scores indicate increasing severity with scores of 5, 10, 15, and 20 representing mild, moderate, moderately severe, and severe depression, respectively. The PHQ9 has good internal consistency and good test-retest reliability [6].

ENRICH marital inventory was utilized given that it is a brief yet reliable and valid tool to measure marital satisfaction in couples [7]. The questionnaire includes 15 items that assess individual and dyadic perspectives on marriage quality [7]. The test is consistent with other forms of marital satisfaction tests. In addition, it includes an Idealistic Distortion component to correct for the variable concepts of marriage in individuals [7]. Increasing scores were indicative of increasing marital satisfaction.

SAS v.9.3 (SAS Institute, Cary, NC) was used for all analysis. Summary statistics, including age, race, education level, annual household income, and pregnancy outcomes, were calculated for the patient population. Responses to the GAD-7 and PHQ-9 questionnaires were scored according to previously published methodology and all participants were classified according to presence and severity (none, mild, moderate, severe) of anxiety and/or depression as indicated by their scores [5,6]. These proportions were compared between sexes using chi-square tests or Fisher's exact tests where appropriate. Jonkheere-terpstra tests were used to measure the change in depression and anxiety over time. Marital satisfaction was measured using the ENRICH questionnaire as described, and all responses were scored using validated methods [7]. To assess change in marital satisfaction over treatment cycle, a repeated measures regression model was used to analyze the scores from the ENRICH questionnaire. Significance level was set at α=0.05 for all analyses.

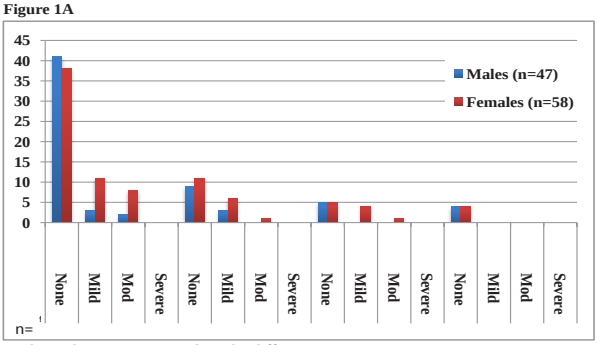
Table 1: Summary Statistics of Study Population.

	Males n=47 (%)	Females n=58 (%)
Race		
Caucasian	37 (78.7)	48 (82.8)
African American	3 (6.4)	4 (6.9)
Hispanic	3 (6.4)	3 (5.2)
Native American	2 (4.3)	1 (1.7)
Asian	2 (4.3)	2 (3.5)
Highest education		
High School	5 (10.6)	4 (6.9)
Vocational School	3 (6.4)	3 (5.2)
Some college	15 (31.9)	14 (24.1)
Undergraduate degree	13 (27.7)	23 (39.7)
Graduate degree	10 (21.3)	14 (24.1)
Missing data	1 (2.1)	0 (0)
Couple's Annual income; $K		
20-40	8 (13.8)	
40-60	13 (22.4)	
60-80	14 (24.1)	
80-100	7 (12.1)	
100-120	3 (5.2)	
120-140	2 (3.4)	
>140	7 (12.1)	
Missing Data	4 (6.9)	
Initiated infertility treatment		
Yes	18 (31.0)	
No	40 (69.0)	
Achieved Pregnancy		
Yes	8 of 18 (44.4)	

Results

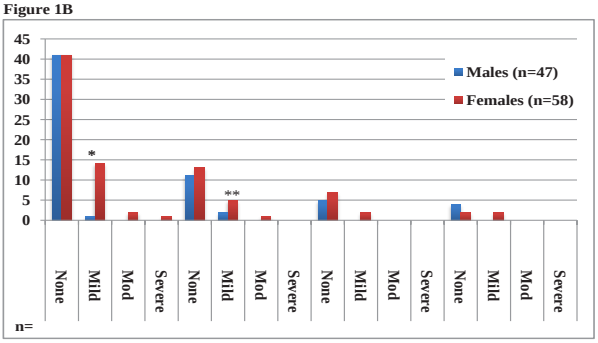
Fifty-eight couples enrolled in the study; all 58 females completed questionnaires but only 47 males completed questionnaires. The average age of the male partners was 32.9±6.8 years old and the average female age was 30.6±SD 4.8 years old. Approximately 80% of both males and females were white, and most had at least some college education (83% and 88% for men and women, respectively). Half of the couples earned between $40,000 - $80,000 per year, and only 15% had an annual household income less than $40,000. Summary statistics are reported in Table 1. Eighteen of 58 couples initiated treatment. When comparing self-reported anxiety with anxiety based on the GAD-7, there was no difference between the two measures in females (p=0.188).However, males reported anxiety less than were found based on GAD-7 questionnaire scores (p=<0.001). Although females (9 of 58; 15.5%) self-reported anxiety at baseline more often than males (1 of 47; 2.1%), this did not reach statistical significance (p=0.16). Additionally, when comparing the incidence of anxiety based on GAD-7 between males and females, there was no difference at baseline or in any individual cycle. For both males and females, the proportion of those with anxiety did not change from baseline with subsequent treatment cycles (p=1.000 and

Figure 1A



Mod= moderate; no statistical gender differences;

Figure 1B



Mod=moderate; * p=0.02 gender difference at baseline; ** p=0.045 gender difference at Cycle 1

Figure 1: Anxiety and Depression in Males and Females at Baseline and During Fertility Treatment; A. Anxiety, as measured by GAD-7; B. Depression, as measured by PHQ-9.

p=0.968, respectively). However, when including only the baseline and cycle 1 survey responses, women had a significant increase in % of those with anxiety at cycle 1compared to baseline (p=0.0154). Notably, only 10 couples completed the second treatment cycle and 4 couples completed the third treatment cycle (see Figure 1A). Although females (8 of 58; 14%) reported depression at baseline more often than males (1 of 47; 1.8%), this did not reach statistical significance (p=0.14). The proportion of females with self-reported depression was less than the proportion with measured depression based on PHQ-9 scores (14% vs. 29%, respectively, p=0.002). There was no difference in male self-reported depression and measured depression (p=1.000). A higher proportion of females had measured mild depression than males at baseline (p=0.02) and at cycle 1 (p=0.045). There was no change from baseline over treatment cycles in male depression (p=0.406). Depression in women also did not change from baseline over treatment cycles (p=0.894) (see Figure 1B). Marital satisfaction as measured by the ENRICH survey showed that there was no difference in marital satisfaction by sex at baseline or with any individual treatment cycle (Table 2).

Discussion

Currently, the literature regarding psychiatric morbidities in patients undergoing Assisted Reproductive Therapies (ART) focuses largely on the female patient only [4] and is specific to those undergoing determined treatment plans [4-6]. Furthermore, time points assessed for morbidities such as depression and/or anxiety in fertility treatment, are quite variable in the literature, proving great difficulty in assessing a temporal relationship or relevancy, if any, to assisted reproductive therapies themselves. With the present study

Table 2: ENRICH Marital Satisfaction Scores at Baseline and During Treatment.

ENRICH score	Male (n=47) (mean, ±SD)	Females (n=58) (mean, ±SD)	p Value
Baseline	52.34±9.05	51.78±9.47	0.75
Cycle 1	46.18±38.61	54.12±50.08	0.06
Cycle 2	46.99±10.78	50.21±17.30	0.71
Cycle 3	46.83±12.81	55.41±5.47	0.14

SD= Standard Deviation

we examined the presence and severity of depression and anxiety in both female and male patients, as well as at multiple time points during ART, in an effort to better target both of these paucities in the literature. Given the complex nature of fertility treatment and increased prevalence of psychiatric co morbidities in this population it is difficult to eliminate treatment-related confounding [1,7]. Ismail et al conducted a psychiatric assessment of changes in affect at differing time periods during preparation and procedure for a Frozen Embryo Transfer (FET). In this study of couples undergoing FET they found anxiety scores unchanged for all visits and between sexes [6]. In contrast, our study had baseline evaluation prior to infertility evaluation by the physician and beginning fertility treatment. By targeting the new infertility consult cohort, we had the ability to assess baseline levels of psychiatric dysfunction prior to consultation with a physician as opposed to literature assessing those patients already accepted for determined treatments such as FET or IVF [9-11]. Utilizing a pre-evaluation and/or treatment start time exercises an effort to avoid undue bias associated with physician interaction and the emotional changes associated with evaluation and treatment of infertility. Thereafter, repeating the screening tests during Cycles 1, 2, and 3 allowed us to observe any change in depression or anxiety that may have developed (or improved) over the course of treatment, regardless of the specific treatment method [9-12]. In our study, we did note a statistically significant increase in mild anxiety in females upon initiating fertility treatment. Regarding variation of psychiatric co morbidities between sexes, specifically depression, and our results highlighted the current data suggesting an increased predominance of depression in women [1]. In utilizing the PHQ-9 to screen for major depressive disorder, we found a higher proportion of women displaying mild depression than men at baseline and this remained during Cycle1. However, there was no change over treatment cycles in male or female depression. Wang et al [13] found that women undergoing IVF are more anxious and emotionally stressed than people in the general population. However, it is hard to say whether the treatment was causing the anxiety and depression because the questionnaires were given while in treatment with no baseline evaluation. Additionally this study enrolled only the women undergoing IVF and not their male partners. Verhaak et al [3] evaluated patients about to start IVF stimulation with gonadotropins and then evaluated those three weeks after pregnancy test. Not surprisingly, the study found that non-pregnant patients had higher depression. There was no change in anxiety in those that achieved pregnancy compared to those that did not. Our results suggest that marital satisfaction does not change during the course of fertility treatments in either sex. Furthermore, it appears that going through all three cycles without conceiving does not play a role in marital satisfaction reporting. There has been limited research that has looked at marital satisfaction in couples undergoing fertility treatments with varying results [15]. Our study is the one of a select few that uses ENRICH marital satisfaction surveys. At the time of this publication it is the only fertility study to administer the survey

to the male partner in addition to the female. Our study looks at marital satisfaction before infertility evaluation or treatment is administered, whereas most studies gather data after completion of a particular treatment cycle. This is an important distinction because treatment success or failure can greatly impact results of scoring marital satisfaction. Most studies on marital satisfaction have focused on couples undergoing treatments in ART such as IVF or FET and not on less aggressive treatments such as intrauterine insemination and many of the studies were given after the pregnancy outcome was known, which could directly impact the couples' answers. Wang et al [13] compared women undergoing IVF or IVF with Intracytoplasmic Sperm Injection (ICSI) to women attending a gynecology clinic and found that undergoing fertility treatment had negative correlation with marital quality. Although we do not know about marital satisfaction in those that discontinued treatment, there was no statistical difference in marital satisfaction between sexes in those that underwent treatment. This is in contrast to previous studies, which have found that men have increased marital satisfaction overall compared with women [14,15]. No absolute conclusion can be drawn from our study due to small sample size. Our study has some strengths and weaknesses that are worth noting. This was a pilot study and therefore underpowered to show some of the differences. We were unable to make comparisons between the specific infertility diagnosis and the measured depression, anxiety, and marital satisfaction. Additionally, there was a high dropout rate from fertility treatment as is expected in all fertility clinics. The baseline levels of both objectively measured anxiety and depression are higher than what is reported in the literature [1], which could be due to a selection bias of, subjects willing to participate in the study. The strengths of this study include enrollment of both the male and the female partner, as the male has usually not been evaluated in similar studies. Anxiety, depression and marital satisfaction were measured using standardized tools. Additionally, changes in marital satisfaction have rarely been looked at in couples undergoing fertility treatment and specifically it has rarely been evaluated in the male partner. Finally, the validated tools were administered mid-cycle of fertility treatment rather than at the completion when pregnancy outcome could affect the results. The impact of anxiety and depression on infertility patients, treatment and likely quality of life cannot be understated. Depression and anxiety should be screened for and acknowledged in couples presenting for infertility evaluation and proper referrals should be made when clinical anxiety or depression are identified. There is evidence that treatment of these disorders could potentially help couples coping with the stress and burden of infertility and fertility treatments [16]. It was encouraging that marital satisfaction did not change during the course of fertility treatment. Future studies with larger number of couples are necessary to further elucidate these relationships.

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