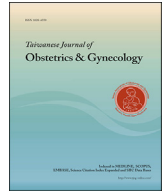




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Original Article

Association of emotional distress and quality of sleep among women receiving in-vitro fertilization treatment

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ABSTRACT

Objective: Sleep disturbance is a common issue that can arise from emotional distress. Women who received the complicated invasive in-vitro fertilization (IVF) procedures can be stressful. The purpose of this study is to understanding the association between emotional distress (measured as anxiety and depression) and sleep quality for women undergoing IVF treatment.**Materials and methods:** This research was of a cross-sectional questionnaire design. Questionnaires were completed during the controlled ovarian hyperstimulation of IVF treatment. A total of 97 participants complete the survey. The questionnaires included basic personal information, The Chinese Traditional Childbearing Attitude Questionnaire, Pittsburgh Sleep Quality Index (PSQI), and the Beck depression and anxiety scales.**Results:** A total of 42.9% and 30% of the participants were determined to be anxious and depressed, respectively. Some participants (18.8%) required more than 30 min to fall asleep, and 56.2% of the participants had less than 7 h of sleep, 43.6% of the participants had less than 85% of sleep efficiency, and 43.3% of the participants were determined with poor sleep quality (PSQI>5). The linear regression analysis indicated that the score of the Beck anxiety index was significantly associated with sleep quality ($F = 44.85$, $p = .000$, adjust $R^2 = 49.4\%$).**Conclusion:** This study revealed that some women when receiving early stage IVF treatments were anxious, depressed, and have sleep disturbance. Anxiety was significantly associated with sleep quality. It is suggested that medical care professional should understand these common issues when assisting women undergoing these complicated reproductive treatments.© 2018 Taiwan Association of Obstetrics & Gynecology. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Infertility is characterized by the failure to establish a clinical pregnancy after 12 months of regular unprotected sexual intercourse, or the impairment of a person's capacity to reproduce either

as an individual or with his/her partner [1]. Women who experienced infertility may result in negative emotional responses, such as low self-esteem, body image disturbance, dissatisfied marriage relationship, depression and anxiety [2,3]. Moreover, Chinese traditional childbearing attitudes could play an important factor affecting psychological distress of infertile women in Taiwan [4]. The global rates of primary and secondary infertility among women aged 20–44 years are 1.9% and 10.5%, respectively [5]. Approximately 3% of infertile couples will seek treatments with assisted reproductive technology (ART). In vitro fertilization (IVF) accounts for 99% of ART treatment with a success rate of 20% [6]. According a Taiwanese report, the 2015 ART included 29,720 cycles with 98% of

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IVF a total pregnancy rate of 44%, and a cumulative live birth rate of 32.5% [7].

Although IVF can give hopes to infertile women, the repetitive complicated invasive procedures can also be an emotional and physical burden for the patients, resulting in psychological distress such as anxiety, depression and sleep disturbance [4,8–11]. The different phases in the treatment process had various aspects of the emotional distress [3,12]. About 20% of the women had clinical signs of anxiety and depression at the beginning of the IVF treatment [13]. Merari et al. indicated women experienced high level anxiety and depression at the oocyte pick-up and before pregnancy test [14]. Moreover, psychological distress was significantly associated with reduced pregnancy chances of ART [12].

Sleep is a calming and serene physiological process that can restore the depletion of physical and mental energy. Sleeping disturbance can include sleep interruption, irregular sleep-wake syndrome, overly-long or short sleeping time, circadian disorder, or hypoxia [15]. Women with changing hormonal levels during menstrual cycle or pregnancy may have affected sleep cycle or sleep disturbance [16,17]. Sleep disturbance may also interfere with women's reproductive processes, such as prolonged conception time, decreased chance of conception, increased rate of miscarriage, and low infant birth weight [15]. Therefore, the sleeping conditions of women undergoing IVF treatment with increased emotional distress need to be better understood to improve ART outcomes.

Lin et al. revealed that 23% and 46% of women receiving IVF presented sleep disorder during the egg retrieval and implantation process, respectively [8]. Goldstein et al. determined that 57%, 43%, and 29% of women receiving IVF were found with sleep disorder during the pre-treatment, stimulation, and post embryo transfer (ET) process, respectively. It was determined that hormone such as anti-mullerian hormone (AMH), follicle stimulation hormone (FSH), and pre-treatment baseline total sleep time (TST) can affect the patient's sleep during the egg retrieval process [9].

Emotional distress and sleep disturbance could contribute to the success of IVF treatment. Therefore, the ovulation induction period (hormonal stimulation) of IVF treatment is the critical time to evaluate the status and association of those psychological distress. However, the literature exploring this issue is scarce. The purpose of this study aimed to (1) investigate the status of emotional distress (anxiety, depression) and sleep quality of women at receiving hormonal stimulation phase of IVF treatment, and (2) examine the associated factors that predict sleep disturbances among women receiving hormonal stimulation phase of IVF treatment.

Material and methods

Subjects

This study was a cross-sectional design with female participants who received IVF-ET between January 2007 and October 2007, in a fertility clinic in middle Taiwan. The study questionnaires were completed at the 5th to 10th day (hormonal stimulation) of the IVF treatment phase. One hundred participants were collected and a total of 97 effective samples were eventually included because 3 women declined participation in the study. This study was approved by the institutional review board (No. CS06101). The researchers had explained the purpose of the study to the participants. The participants could withdraw at any time without any effect to the quality of their medical treatment. The surveys were performed after obtaining consent from the participants. The inclusion criteria were women with primary infertility. Women with secondary infertility and using donor sperm were excluded.

Instruments and tools

The study tools were structured questionnaires that included basic personal information, Chinese Traditional Childbearing Attitude Questionnaire, Beck depression and anxiety scales and Pittsburgh Sleep Quality Scale.

Basic personal information included: age, education, occupation, economic status, cause of infertility, infertility time, the number of times receiving ART, desire to reproduce [4].

The Chinese Traditional Childbearing Attitudes Questionnaire (CTCAs) was developed and used by Lee and associates [4] based on Chinese culture and experiences. CTCAs include the following items: (a) having no heir is the gravest offense against filial piety, (b) continuing the family line is a mandatory responsibility, (c) raising children is insurance against the insecurity of old age, (d) having children means having more good fortune, (e) three generations living together is desirable, and (f) a son is more important than a daughter. A three-level scoring system was used for data analysis: for each attitude: 2 points were assigned for the answer of "agree"; 1 point for the answer of "somewhat agree"; and 0 point for the answer of "do not agree". The final scores could range from 0 to 12. The authors subsequently divided the total scores into 3 groups of childbearing attitudes differentiating the levels of CTCAs. The range for scores of 0–4 indicated weak level of childbearing attitude, 5–8 indicated medium level of childbearing attitude, and 9–12 indicated strong level of childbearing attitude. The Cronbach coefficient α (reliability) of the questionnaire in this study was 0.73.

The Beck Anxiety Inventory (BAI, Chinese version)– a self-report measure of anxiety authorized and published by the Chinese Behavioral Science Corporation in Taiwan. There are 21 questions in the Beck anxiety inventory that measures the symptoms of anxiety. The publication in 1988 by Beck described the symptoms of anxiety as: numbness or tingling of body, hot flash, unsteady feet, cannot relax, fear the worst thing will happen, dizziness, loud or fast heartbeat, unstable, unease, horrified, nervous, feeling of suffocating, trembling, fear of losing control, difficulty breathing, fear of imminent death, panic, indigestion, fainting, blushing, and sweating. Each question is scored from 0 to 3 with increasing severity. A score from 0 to 7 are "slight", 8 to 15 are "mild", 16 to 25 are "moderate", and 26 to 63 are "severe". The BAI has a good internal consistency (Cronbach's α was 0.92) and reliability (one-week retest reliability was 0.75) [18]. The reliability of Cronbach α in this study was 0.93.

The Beck Depression Inventory (BDI-II, Chinese version)– a self-reported depression scale authorized and published by the Chinese Behavioral Science Corporation in Taiwan. There are 21 questions in the BDI with depression indications such as: mood, pessimism, sense of failure, discontent, guilt, self-esteem, self-control, suicidal desire, crying, perplexity, social retreat, indecision, distorted body image, low work drive, sleep disorder, fatigue, loss of appetite, weight loss, excessive attention to the body, and lower sex drive. Each question is scored from 0 to 3 with increasing severity. A score from 0 to 13 are "normal", 14 to 19 are "mild", 20 to 28 are "moderate", and 29 to 63 are "severe". The BAI has a good internal consistency with Cronbach's alpha range between 0.70 and 0.93. The BDI is the most commonly used self-reported depression test that has been translated to different languages and is widely used around the world [19]. The reliability of Chronbach α in this study was 0.89.

The Pittsburgh Sleep Quality Index (PSQI)– a self-report test that determines the sleep qualities of the subject with 7 sections. These sections are: (1) subjective sleep quality; (2) sleep latency; (3) sleep duration; (4) sleep efficiency; (5) sleep disturbance, (6) use of sleep medication, and (7) degree of daytime dysfunction.

There are a total of 19 questions with scores that can range from 0 to 21. The global sum of “5” as the boundary of good sleep quality, where subject with a score over 5 is determined with sleep disorder and vice versa [20,21]. It was demonstrated by Buysse et al. [20] that the index's validity and reliability were $\alpha = .83$ and $\gamma = 0.85$, respectively. The reliability of Chronbach α in this study was 0.81.

Statistical analysis

The obtained data were entered into the computer and analyzed with SPSS/PC Window 17.0. The distribution of variables were $n(\%)$ and mean(SD) for descriptive statistics. The inferential statistics included X^2 , Pearson correlation, and stepwise linear regression. The dependent variable was scores of PSQI. The independent variables included age, education, length of infertility, frequency of IVF treatment, CTCAs, BDI and BAI. The level of significance was $\alpha < 0.05$.

Results

Most of the participants were older or equal to 35 years of age (62.9%) with an average age of 35.7 years (SD 5.29); had college or high educational levels (70%), had less than 48 months of infertility (43.3%) with an average infertility duration of 51.5 months (SD 36.5); had average IVF treatments of 2.5 times (SD 2.1); and with medium or high desire to reproduce (82.2%). From the BAI analysis, 23.1% and 19.8% of the participants were determined with mild anxiety and moderate to severe anxiety, respectively. From the BDI analysis, 18.9% and 11.1% of the participants were found with mild depression and moderate to severe depression, respectively (Table 1).

In the sleep quality index analysis, most of the participants had poor and very bad subjective sleeping quality (30%). Some required more than 30 min to fall asleep (18.8%), most participants had less than 7 h of sleep per day (56.2%), 43.6% of the participants had sleep efficiency rates lower than 85%, most of the participants did not use medications as sleeping aid (94.8%), most of the participants had daytime dysfunction (74.2%), and the participants with poor sleep qualities (PSQI total scores > 5) were 43.3% (Table 2).

Table 3 showed the Pearson correlation among variables. Age had positive correlation with income ($r = 0.25$, $p < 0.05$), length of infertility ($r = 0.46$, $p < 0.01$), and frequency of IVF treatment ($r = 0.38$, $p < 0.01$). The longer the infertility time, the more IVF treatments ($r = 0.65$, $p < 0.01$) a woman required. Anxiety had strong positive correlation with depression ($r = 0.57$, $p < 0.01$). The score of PSQI had strong positive correlation with anxiety ($r = 0.57$, $p < 0.01$) and depression ($r = 0.54$, $p < 0.01$) (Table 3).

It is demonstrated in Table 4 that participants with poor and good sleep quality exhibited average BAI scores of 11.9 and 5.3, respectively, with statistical significance ($p = 0.001$). The BDI scores among the poor and good sleepers were 12.3 and 6.4 ($p = 0.057$) (Table 4).

The linear regression analysis of sleep quality determined that BAI is a major predicting factor ($F = 44.85$, $p = 0.000$, $R^2 = 50.5\%$, adjust $R^2 = 49.4\%$) for sleep quality (Table 5).

Discussion

This research was conducted to explore the levels of anxiety, depression and sleep quality of women at receiving hormonal stimulation phase of IVF treatments. We also examined the associated factors that predict sleep disturbances among women receiving hormonal stimulation phase of IVF treatment. The study results indicated that 42.9% of the women were with mild to severe anxiety, and 30% of the women were with mild to severe depression. The prevalence rates of anxiety and depression in our study

Table 1
Baseline demographics and clinical characteristics of the enrolled participants (N = 97).

Characteristics	n	%	Mean \pm SD
Age(y)			35.7 \pm 5.29
<30	7	10	
30–34	19	27.1	
≥ 35	44	62.9	
Education			
Junior high school less	6	6.3	
Junior high school	23	24	
College or above	67	69.8	
Income US dollars(per month)			
≤ 1250 USD	10	10.4	
1250–1875 USD	33	34.4	
1875–2500 USD	18	18.8	
2500–3125 USD	18	18.8	
> 3125 USD	17	17.7	
Length of infertility(Month)			51.5 \pm 36.5
<48	42	43.3	
48–95	25	25.8	
≥ 96	30	30.9	
Frequency of IVF treatment			2.5 \pm 2.1
1	35	36.5	
2	26	27.1	
≥ 3	35	36.5	
Attitude of childbearing			7.6 \pm 3.2
0–4	17	17.9	
5–8	39	41.1	
9–12	39	41.1	
BDI			10.2 \pm 8.2
0–13 Normal	63	70	
14–19 Mild	17	18.9	
20–28 Moderate	8	8.9	
29–63 Severe	2	2.2	
BAI			9.3 \pm 9.1
0–7 Slight	52	57.1	
8–15 Mild	21	23.1	
16–25 Moderate	12	13.2	
26–63 Severe	6	6.6	

BDI: Beck Depression Inventory.

BAI: Beck Anxiety Inventory.

were higher than Reading's study [13]. Undergoing an IVF treatment involves experiencing multi-dynamic distress. At the beginning of treatment phase, women received multiple ovarian hyperstimulation drugs, blood tests and underwent ultrasound scans regularly to monitor the growth of follicles [2]. Women were likely to describe the IVF procedure as moderately stressful [22]. Regardless of the first or repeated IVF treatment, all of the patients exhibited anxiety during the procedures [10].

The results of this study indicated that nearly 1/5 of patients were with sleep latency of greater than 30 min at the beginning of the treatment phase. A total of 43.6% of the women exhibited sleep efficiency rates lower than 85%, and 43.3% of the women exhibited sleep disturbance (PSQI total scores > 5). It means that women suffered from sleep problems during the IVF treatment. These findings were very similar to those studies of Goldstein et al. and Lin et al. [8,9]. The rate of sleep disorder among the patients also seemed to fluctuate with the treatment cycle, in which 23% of the women reported poor sleep during egg retrieval, while 46% and 29% had similar sleep problems before and after embryo transfer, respectively. The patient's initial state of sleep may also affect the quality of sleep during the later stage of treatment [9]. The review article by Kloss et al. has investigated relationships among sleep, sleep disturbance, and women's reproductive health. The authors proposed that sleep disorder may be an individual's physiological response to perceive the real threats, which can further affect fertility. Therefore, sleep disorder can be more severe when infertile women are receiving ART treatments [15].

Table 2
Sleep quality of participants (N = 97).

	n	%
Subjective sleep quality		
Very good	8	8.2
Fine	60	61.9
Poor	23	23.7
Very Bad	6	6.2
Sleep latency		
(1) The time spent before going to sleep		
≤ 15 min	31	32.3
16–30 min	47	49
31–60 min	12	12.5
≥ 61 min	6	6.3
(2) Cannot get to sleep within 30 min		
Never	32	33
<1/week	27	27.8
<2/week	23	22.3
<3/week	15	15.5
Sleep duration		
≥ 421 min	42	43.8
361–420 min	39	40.6
301–360 min	12	12.5
≤ 300 min	3	3.1
Habitual sleep efficiency		
≥ 85%	53	56.4
75–84.9%	27	28.7
65–74.9%	9	9.6
≤ 64.9%	5	5.3
Sleep disturbances		
0 point	3	3.3
1–9 points	59	64.8
10–18 points	26	28.6
19–27 points	3	3.3
Use of sleeping medication		
Never	92	94.8
<1/week	1	1
1–2/week	2	2.1
>3/week	2	2.1
Daytime dysfunction		
0 point	25	25.8
1–2 points	37	38.1
3–4 points	27	27.8
5–6 points	8	8.2
Total score		
≤ 5 Good quality	51	56.7
>5 Poor quality	39	43.3

This study indicated that the average scores of anxiety between the two groups (patients with good vs. poor sleep quality) were both significantly different, whereas the average depression scores were only approaching significance. The stepwise linear regression for prediction of the sleep quality indicated that anxiety scores could significantly affect the sleep quality, with R^2 accounted for 49.4% of the association. This result suggests a strong degree of correlation between emotional distress and sleep disturbance.

Table 3
Pearson correlation among variables.

Items	1	2	3	4	5	6	7	8	9
1 Age	1								
2 Education	0.64	1							
3 Income	0.25*	0.55**	1						
4 CTCAs	0.04	0.1	0.22*	1					
5 Length of Infertility	0.46**	−0.1	0.01	−0.14	1				
6 No. IVF treatment	0.38**	0.05	−0.05	0.01	0.65**	1			
7 BDI	−0.13	−0.12	−0.13	−0.06	0.12	0.13	1		
8 BAI	−0.12	−0.12	0.23*	−0.08	−0.14	0.17	0.57**	1	
9 PSQI	−0.07	0.03	−0.03	−0.07	−0.06	0.04	0.54**	0.57**	1

* $p < 0.05$.** $p < 0.01$.

Anxiety and sleep disturbance may have “comorbid” relationship in which anxiety and sleep disturbance can affect each other. Similar result can also be observed in different groups of patients such as pregnant women, and physically or mentally ill patients. The research performed by Volkovich et al. suggested that emotional distress (i.e., the severity of depressive and anxiety symptoms) during pregnancy is associated with subjective sleep disturbances but not with objective sleep disturbances [23]. Literature indicated that both anxiety and sleep disorder can affect the fertility outcomes of women [12,15]. Therefore, for the goal of treating infertility, the mental health status of the patient should also be considered. The improvement of both physical and mental health of the patient should be the ultimate goal for the health care professionals. Sleep may be an adjustable factor that can be affected by medications. However, 94.8% of the participants did not use medication for sleep. This result may be due to cultural or the increased medication intervention used during the IVF treatment. The medical care staff could consider non-medical methods for improving the sleep quality of these patients such as cognitive behavioral therapy, bedtime ambient light adjustments, physical and mental relaxation therapy, and the use of music to achieve the purpose of relaxation [24–26].

Last, most infertile women were older age with the average age of 35.7 years in this study, and 63.5% of the patients received repeated treatment. Positive correlation was found between age, length of infertility and frequency of IVF treatment. Women had to face with the last hope of pregnancy by means of IVF treatment and the fact that lower pregnancy rate is associated with advanced age [5]. In this growing trend of delayed marriage around the world, age solely can impose reproductive challenges for the couples and the advanced age of women is especially associated with the decreased fertility rate [5,7]. Therefore, the medical care staff should actively provide more information on fertility education not only to infertile couples but also to the public.

The main advantages of this study is the use of simple scales for understanding the anxiety, depression, and sleeping qualities of women receiving IVF treatment. This study demonstrated a high “comorbid” relationship between anxiety and sleep disorder. The measurements of this study were performed at the hormonal stimulation phase of IVF treatments, where it could provide information for the health care professionals in the early detection of psychological stress and sleep conditions of the patients. The results can provide early assistance for patients receiving IVF treatments.

There are some limitations in this study. First, the number of cases is small. Second, the psychological stress response and sleep status measurement are subjective descriptions by the cases without the objective information. Third, there is no control group. Therefore, it is suggested that future studies should increase the number of cases, include objective measurement of sleep quality (such as stress physiological indicators and actigraphy), and establish control groups for an improved investigation.

Table 4
Sleep quality and mean scores of BDI/BAI.

	BDI					BAI			
	n	Mean ± SD	t	p		n	Mean ± SD	t	p
Sleep quality									
Good	33	6.4 ± 5.6				36	5.3 ± 5.7		
Poor	51	12.3 ± 8.5	−3.82	0.057		49	11.9 ± 9.4	−4.1	0.001

Table 5
Stepwise linear regression for predicting PSQI with women who received IVF treatment.^a

Variable	B	SE	95%	CI	p
			Upper	Lower	
Constant	4.15	0.53	3.08	5.22	0.000
BAI	0.27	0.04	0.19	0.34	0.000

Independent variables: age, education, income, length of infertility, frequency of IVF treatment, CTCAs, BDI, BAI.

^a F = 44.85, P = .000, R² = 50.5% (adjust R² = 49.4%).

Clinical implication

This study revealed that most women receiving IVF treatments were anxious (43%), depressed (30%), and have troublesome sleeping (43%). Anxiety is especially related with sleeping disturbance. It is suggested that medical care professional should understand these common issues when assisting women undergoing these complicated reproductive treatments. Implements such as mental health assessment and sleep history can be used to provide a more comprehensive model of care.

Authors' contributions

Study conception and design: LHH, YCL, CPK, MSL, and SHL. Data collection: LHH, and SHL. Analysis and interpretation of data: LHH, and SHL. Drafting of manuscript: LHH, MSL, and SHL. All authors read and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

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