

Anxiety (DASS21) and the Quality of Life (FertiQol) of Infertile Women Underwent In Vitro Fertilization

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Abstract

Infertility affects physical and mental health and has various consequences. In vitro fertilization (IVF) is one of the Assisted Reproductive Technology (ART) programs that include several phases, requiring longer time, more patience, and is expensive. This may make women who undergo the ART program to have higher stress level, especially anxiety. This study aimed to determine the relationship between anxiety and quality of life in infertile patients undergoing assisted reproductive technology programs. This was a cross-sectional observational analytic study performed at Aster Fertility Clinic, Dr. Hasan Sadikin General Hospital and Bandung Fertility Center, Limijati Hospital Bandung, Indonesia, from February until April 2020. The analysis was performed using the DASS21 scale and FertiQol count on 27 subjects undergoing the IVF program and 30 control subjects who were pregnant without IVF program. The statistical analyses used to determine the condition of anxiety and the condition of quality of life were the Chi-square and the Mann-Whitney tests, while the relationship between anxiety and quality of life as the main subject was measured using the Spearman correlation test. The anxiety level as measured with the DASS21 instrument in the subject and control groups was 6.2 vs 0.7 with $p < 0.001$. From the analysis of the FertiQol instrument in the subject and control groups, the scores were 79.6 vs. 98.9 for the mind-body domain ($p < 0.001$); 68.8 vs 98.5 for the emotional domain ($p < 0.001$); 83.2 vs 95.7 for the relational domain ($p < 0.001$); and 77.6 vs 97.6 for the social domain ($p < 0.001$). For the overall FertiQol core domains, the score was 77.3 vs 97.7 ($p < 0.001$). The correlation between anxiety and the FertiQol total core domains were evident from the results of the Spearman correlation test, with an r -value of -0.479 ($p < 0.001$). Therefore, there is a significant negative correlation between anxiety and quality of life.

Keywords: Anxiety, infertility, quality of life

Introduction

Reproduction is one of the most essential elements in life, and failure of this process can be a severe physical and mental health problem. Infertility is not easily seen, but it is common among reproductive age groups today. Infertility means the inability to have offspring after marriage for more than one year without using a contraceptive. Infertility is known to be a psychosocial problem in itself. It potentially has profound consequences that cover various aspects affecting socio-cultural, emotional,

physical, and financial problems. The World Health Organization (WHO) evaluation of Demographic and Health Surveys (DHS) data found that more than 186 million married women of reproductive age in developing countries dream of a child. This means 1 in every four couples in developing countries.^{1, 2} In Indonesia, according to the Central Agency of Statistics, in 2011, there are 10–15% cases of infertility from nearly 40 million women of childbearing age.³ The factors that cause infertility are very diverse and complex; therefore, many fertility therapies are carried out following the cause of infertility. In vitro fertilization (IVF) is one of the assisted reproductive technology, at this stage fertilization between sperm and ovum, is not carried out naturally but requires a lot of time. This procedure has many several phases. The first phase consists of taking the mature oocytes in the ovaries,

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which will be brought together with sperm in the laboratory, and transferring the embryos into the uterine cavity. These oocytes are grown by stimulation of gonadotropin hormones. This stimulatory response can vary and sometimes takes more time. If the stimulation is successful, transvaginal ultrasound guidance of follicular oocyte retrieval after stimulation also takes time. After that, it will be examined under a microscope to assess its quality level before fertilization. The stages of in vitro fertilization are expensive, can be a long-time treatment, and need more patience with uncertain final results.⁴ This makes the program so special because both before and after the program can put the patient under psychological pressure. Studies show that anxiety symptoms increase by almost 10% in patients undergoing this program.⁵

Many factors related to infertility make this a problem in itself which often causes stressors. It is not uncommon for a related partner to be prone to stress related to infertility such as stress when knowing the cause of infertility, disturbance or discomfort during intercourse with a partner or while undergoing a long series of fertility therapy.⁶ A long series of fertility therapies is prone to placing patients in psychological conditions such as stress, and found that infertility therapy is the most stressor factor in infertile women.⁷ Moreover, the National Health Insurance (JKN) program in Indonesia does not include fertility service as one that can be covered.

The number of people with mental disorders generally increases every year, especially in low-income countries, because population growth is taking place and most people are of reproductive age. Physical health is easier to recognize because it can be complained about, but mental health is still difficult to recognize. This encourages a person to take the necessary steps to prevent the threat or reduce its consequences. Anxiety is one of the most common psychiatric disorders. The population with anxiety disorders in 2015 was estimated to be 3.6% (264 million people) of the world's population. The National Comorbidity Study reports that one in four people will have at least one anxiety disorder. Its prevalence in Southeast Asia is as much as 23% of the world's total population with anxiety disorders. The majority of sufferers are women.⁸

Anxiety can be defined as a normal and adaptive response that has life-saving qualities and warns of threats of damage, pain, helplessness, frustration with physical and social needs; or separation from loved ones. This encourages a person to take the necessary steps

to prevent the threat or reduce its consequences. Anxiety is one of the most common psychiatric disorders. The population with anxiety disorders in 2015 has been estimated to be 3.6% (264 million people) of the world's population. The National Comorbidity Study reports that one in four people will have at least 1 anxiety disorder. Its prevalence in Southeast Asia is as much as 23% of the total population with anxiety disorders in the world. The majority of sufferers are women.⁸

Emotional stress, such as frustration and aggressiveness, depression, and anxiety, impact pregnancy. Those who chose the ART programs tended to have higher distress when compared to infertile women who did not undergo any fertility program and did not try to conceive children.⁹ Lazarus and Folkman¹⁰ emphasize that stress can create positive and negative experiences. Another claimed that there are many negative associations between stress related to infertility. This stressor caused by infertility, also called infertility-related stress, can last quite a long time, even up to a lifetime, so that it can become a chronic stressor affecting various aspects of life such as relationships with partners and the surrounding community, sexual relations, even the desire to become parents.¹¹

This study aims to determine the relationship between anxiety and quality of life in infertile patients undergoing assisted reproductive technology programs. This study can be beneficial as the basis of development for increasing the success of assisted reproductive technology.

Methods

This observational analytic study with a cross-sectional design aims to see the relationship between anxiety and the quality of life of women undergoing IVF in ART clinics. The subjects are the women participating in IVF Aster Clinic Dr. Hasan Sadikin Hospital Bandung and Bandung Fertility Center Limijati Hospital Bandung from February to April 2020. The subject's criteria are women who underwent IVF for the first time, had a history of primary and secondary infertility, and without a history of serious mental disorders or using psychotropic medication. Control subjects are women who have had a pregnancy without undergoing an IVF program and without a history of serious mental disorders or using psychotropic medication. The exclusion criteria are women who refused to follow the research procedure and had previously followed the IVF

program. The selection of subjects was obtained from all patients who came for the IVF program during the period from February until April 2020.

The measuring instrument used is the Depression, Anxiety, and Stress Scale (DASS). This questionnaire is designed to measure harmful emotional levels of depression, anxiety, and stress. Each rating scale consists of 14 points divided into 2–5 sections with the same content. Subjects will be asked to fill out a severity scale ranging from 1 to 4 points. The questionnaire consists of 21 questions. These numbers will be your depression, anxiety, and stress scores, which will be calculated by adding them up.¹²

Another measuring tool is Fertility Quality of Life (FertiQol). This FertiQol was created in 2002 by The European Society of Human Reproduction and Embryology (ESHRE) and the American Society of Reproductive Medicine (ASRM) to identify areas affected by fertility problems. In this questionnaire, several domains can be assessed in a total of 36 questions, divided into two questions to evaluate overall personal physical health, 12 questions to assess the impact of fertility problems on the emotional domain (6 questions), and the mind-body domain (6 questions), 12 questions to measure the impact of fertility problems on relationship domain (6 questions) and social domain (6 questions) and ten questions to measure the quality of life during the program, both intervention and consultation based on environment (6 questions) and

acceptance of the therapy given (4 questions).¹³

This study has received ethical approval from Health Research Ethics Committee Dr. Hasan Sadikin General Hospital with serial number LB.2.01/X.6.5/31/2020. The minimum sample of this study was 25 patients. The data was taken using a cross-sectional research design and analyzed with SPSS. The data collection was obtained through a questionnaire that was filled in and a score was calculated to determine the degree of anxiety and the quality of the research subject. Descriptions of female characteristics are presented in tabular form. Anxiety conditions obtained from the DASS research instrument and quality of life from the FertiQol instrument were processed and described by the number (n) and the percentage (%). The normality test shows that the distribution of study variables is normal. The analysis of this study was conducted using the Chi-square test for categoric criteria and the Mann-Whitney test for the numeric criteria, while the relationship between anxiety and quality of life in the main subject using the Spearman correlation test.

Result

Research has been conducted on 27 infertile women and 30 control women from February to April 2020. This study grouped the characteristics data by age, length of the marriage, and history of abortion.

Table 1 Characteristics of Both Groups

Characteristics	Group		p ^{*)}
	IVF Program (n=27)	Control (n=30)	
Age (year)			0.837
<35	21	24	
≥35	6	6	
Mean (SD)	32.0 (4.4)	28.3 (6.2)	
Range	24–41	19–44	
Duration of infertility (year)			0.161
≤5	17	25	
6–10	8	3	
>10	2	2	
Mean (SD)	5.7 (3.4)	4.0 (4.1)	
Range	1–15	1–18	
History of miscarriage			0.949
Yes	7	8	
No	20	22	

Note: *) Chi-square test

Table 2 Comparison between Anxiety of Both Groups

Anxiety	Group		p ^{*)}
	IVF Program (n=27)	Control (n=30)	
Anxiety score :			<0.001
Mean (SD)	6.2 (3.9)	0.7 (1.2)	
Median	8	0	
Range	0-18	0-4	
Anxiety level:			<0.001
Normal	13	30	
Mild	10	-	
Moderate	3	-	
Severe	1	-	

Note: *) Anxiety score using Mann-Whitney test; Anxiety level using Chi-square test

From the Table 1, both age groups, duration of infertility group, and history of miscarriage group, the results obtained with a $p > 0.05$; this means that both groups have homogeneous data.

It appears that the median score of anxiety in women who attended the IVF program was more different than the control group (8 and 0), and this difference was statistically significant ($p < 0.001$). In the IVF program group, 41.9%

experienced mild to severe anxiety, whereas in the control group, all anxiety levels were classified as normal.

It found a significant difference ($p < 0.001$) between the two study groups for each domain of quality of life. In the group of women who followed IVF, the median quality of life score was lower than the control group

In the IVF program group, the more age

Table 3 Comparison Between Quality of Life of Both Groups

Quality of Life (Domain)	Groups		p ^{*)}
	IVF Program (n=27)	Control (n=30)	
Mind-body			<0.001
Mean (SD)	79.6 (15.2)	98.9 (1.8)	
Median	79.2	100	
Range	58.33-100	95.8-100	
Emotional			<0.001
Mean (SD)	68.8 (19.4)	98.5 (2.0)	
Median	66.7	100	
Range	45.8-100	95.8-100	
Relational			<0.001
Mean (SD)	83.2 (13.3)	95.7 (4.0)	
Median	83.3	95.8	
Range	62.5-100	91.7-100	
Social			<0.001
Mean (SD)	77.6 (17.3)	97.6 (2.1)	
Median	79.2	95.8	
Range	25-100	95.8-100	
Total Core FertiQol			<0.001
Mean (SD)	77.3 (13.0)	97.7 (1.6)	
Median	82.3	97.9	
Range	55.2-100	94.8-100	

Note: *) using the Mann-Whitney test

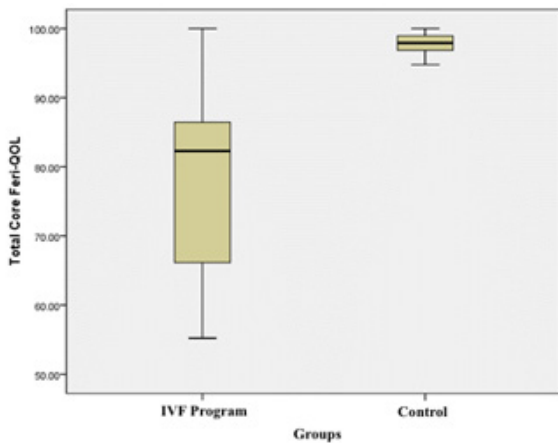


Figure 1 Comparison between the Quality of Life in Both Groups

increases, the more anxiety score increases. In the IVF program group, there was a relationship between age and quality of life, which is significant in mind, body, relational, social, and total core FertiQol; the more age increases, the lower the quality of life score. The correlation between the duration of infertility with anxiety scores and quality of life was not statistically significant ($p > 0.05$). Analysis of the correlation between age and duration of infertility with anxiety scores and quality of life in the control group did not show a significant relationship ($p > 0.05$). The correlation between anxiety scores and total core FertiQol in the IVF program group showed a negative correlation with significant differences (Table 4 and Figure 2); this illustrates the overall correlation between anxiety and quality of life. From this result, the higher the anxiety score, the lower the quality of life.

Discussion

The impact of infertility on the occurrence of psychological distress in a person who experiences it has long been known. The prevalence of anxiety disorders in infertile couples ranges from 25–60%.¹⁴ A meta-analysis study said that anxiety occurs three times more in infertile couples than in fertile couples.¹⁴ Anxiety can occur and is significantly associated with the duration of infertility and level of education. Generally, this anxiety occurs in women who have experienced infertility for 4–6 years.¹⁵ History of miscarriage can be a form of post-traumatic stress disorder as anxiety and depression. Apart from comorbidities and financial factors, it was also found that psychological factors could cause the discontinuation of this IVF program.¹⁶

In Vitro Fertilization program is unique because this program might be a couple's last effort to get pregnant which involves feeling optimistic and full of hope while, as we know, there is always a failure rate. When starting therapy, usually the patient will undergo a series of tests to determine the cause of infertility. Patients who finally choose assisted reproductive technology programs face busy schedules that are time-consuming and long-term and live among hope, fear, and frustration.¹⁷ This method also requires a lot of money, time, and a long and invasive procedure. Turner et al. found that these stress and anxiety levels increased with each stage of the IVF cycle. This can cause higher levels of distress in those undergoing the stages of the IVF program. This is what becomes the point that psychological distress will increase with time.¹⁹ However, there are also other studies

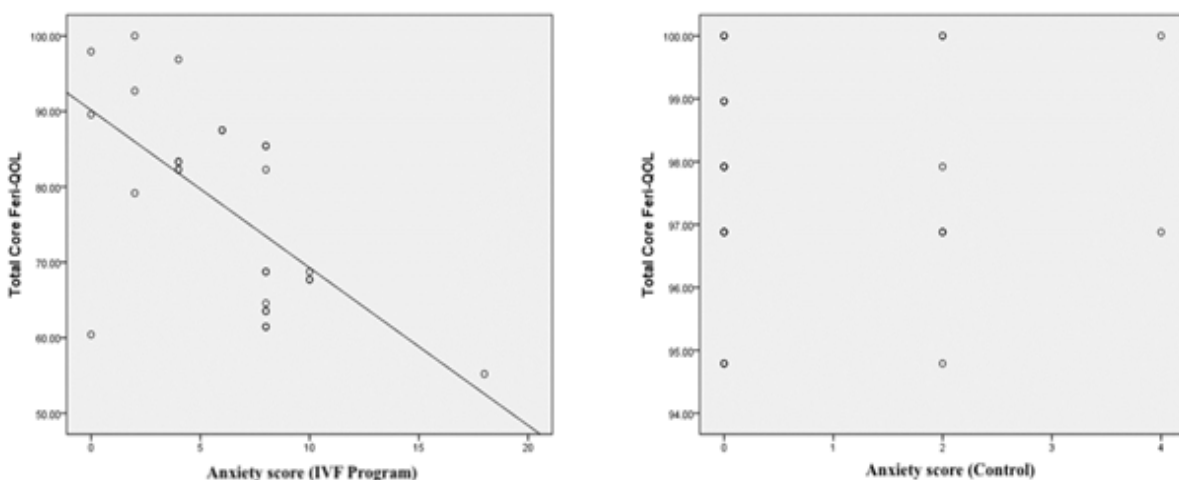


Figure 2 Correlation between Anxiety and Quality of Life in Both Groups

Table 4 Relationships between Age, Duration of Infertility, Anxiety, and Quality of Life in Both Groups

Correlation between	IVF Program		Control	
	r	p	r	p
Age and anxiety	0.503	0.008	0.098	0.607
Duration of infertility and anxiety	0.184	0.357	-0.112	0.555
Age and mind-body	-0.401	0.038	-0.026	0.891
Age and emotional	-0.335	0.087	0.036	0.850
Age and relational	-0.521	0.008	0.213	0.259
Age and social	-0.605	0.001	0.047	0.806
Age and total core FertiQol	-0.547	0.003	0.195	0.302
Duration of infertility and mind-body	-0.241	0.227	0.182	0.336
Duration of infertility and emotional	-0.209	0.296	0.179	0.344
Duration of infertility and relational	-0.263	0.185	0.192	0.309
Duration of infertility and social	-0.317	0.107	0.115	0.546
Duration of infertility and total core FertiQol	-0.295	0.135	0.304	0.103
Anxiety and mind-body	-0.470	0.013	-0.065	0.733
Anxiety and emotional	-0.518	0.006	0.075	0.695
Anxiety and relational	-0.486	0.010	0.092	0.631
Anxiety and social	-0.622	0.001	0.019	0.919
Anxiety and total core FertiQol	-0.585	0.001	0.027	0.886

Note: r = Spearman's rank correlation coefficient

with different results in which women who have been infertile for a long time have lower levels of anxiety and depression. This can occur due to psychological adaptation to infertility.²⁰

Studies have shown that stress, anxiety, and other negative emotions affect pregnancy rates. High-stress levels and low quality of life are associated with low cortisol levels. Cortisol can be a biomarker of the hypothalamic-pituitary-adrenal (HPA) axis. Activating the hypothalamic-pituitary-adrenal (HPA) axis by stimulation of the gonadotropin-releasing hormone (GnRH) will impact a series of hormonal cycles involving reproductive functions.²¹

The World Health Organization defines the quality of life as an individual's perception of his position in life in the context of culture and place of residence concerning the goals, hopes, and concerns at hand. The FertiQol instrument was developed to assess the quality of life specifically for individuals with fertility disorders, regardless of the specifics of fecundity, gender, and social and cultural backgrounds.²² FertiQol has two main components, namely core FertiQol, which includes the relationship between the subject and its surroundings, and treatment FertiQol (optional), which includes the relationship between the subject and fertility therapy. Core FertiQol consists of an individual part, namely the mind/body and emotional domain, and an interpersonal part, namely the relational and social domain. The mind/body domain assesses

how far the experience is from the occurrence of negative physical symptoms (fatigue, pain) and cognitive and behavioral disorders (lack of concentration, disturbances in daily activities, hampered life plans) due to this infertility. The emotional domain assesses how far the individual experience a collection of negative emotions related to infertility (jealousy, hate, sadness, and depression). The relational domain assesses the extent of the impact of fertility problems related to marital or partner relationships (sexuality, communication, commitment). The social domain measures the level of social interaction affected by fertility problems (social inequality, expectations, stigma, and support).¹³

All the core components of FertiQol in this study showed significantly different results between infertile women who underwent the IVF program and control subjects. The difference in the core FertiQol and each component shows a lower value result than the control group. This is evident from previous studies, which found that women with children clearly show a higher quality of life, especially in the mind/body and emotional domains. The duration and causes of infertility are known to be low in the mind/body domain in this measurement.²³

This study also found a significant relationship that the higher the level of anxiety in infertile women, the lower the quality of life. These results are similar to previous studies with different psychological measures and quality of life.²⁴

Although unclear, knowing whether this psychological distress causes infertility is essential. Several studies link this relationship, especially in IVF programs. These studies found that the higher a person's distress, the lower the pregnancy rate,^{25,26} while some other studies say otherwise.²⁷

Psychological interventions to reduce stress can be helpful for all causes of infertility, although the link is unclear. Re-counseling can be very useful in reducing negative effects such as anxiety and infertility-related stress even before starting fertility therapy to reduce tension and worry before fertility therapy is started. Another study even found that this intervention was associated with lower psychological distress and higher pregnancy rates.²⁸ The controversy over this matter is still unclear. Existing studies often have different results. Boivin et al. found that psychological intervention, although it has an impact on reducing adverse psychological effects, has no difference in pregnancy rates.²⁷ The Cochrane review found no evidence that higher pregnancy rates are associated with decreased anxiety.²⁹

Despite their success in increasing pregnancy rates, almost all of these interventions have proved worthwhile as they have improved psychological outcomes and better marital relationships.³⁰ Therefore, researchers argue that by knowing the level of anxiety and quality of life of women who follow the IVF program, it is necessary to play an important role in thinking "how do we feel and what do we do" in challenging thoughts such as never having a baby, infertility as its fault, and husband's infidelity.

A limitation of this study is that the sample only comes from two fertility clinics. The FertiQol questionnaire has a treatment scale that assesses the tolerability of the therapy and the fertility clinic environment. However, in this study, no measurements were made on these domains because the control subjects were fertile women who did not get their pregnancies from the IVF program. Apart from this, it is necessary to identify confounding factors and explore the possibility of existing risk factors that can affect the research results. Also, this study wants to explain why the control group did not compare with the group of infertile patients who did not get an IVF program for some reason because it is challenging to find infertile patients who do not indicate IVF, as it is known that IVF is indicated mainly in tubal factor disorders, unexplained and male infertility.

This study concludes that there are significant

differences in anxiety conditions and quality of life conditions between the patient groups who underwent IVF and controls. There was also a significant relationship between anxiety conditions and quality of life in the group of patients who underwent IVF, that the higher the level of anxiety, the lower the quality of life. Psychological measurement tools such as DASS and FertiQol in fertility clinics need to recommend to obtain psychological information and quality of life that can help overcome fertility problems and adapt better to psychological stress caused by infertility.

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