



# Anxiety Effect in the Success Rate of Intrauterine Insemination (IUI) and *In Vitro* Fertilization (IVF)

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**How to cite this paper:** Syam, H.H., Madjid, T.H., Effendi, J.S., Djuwantono, T., Permadi, W. and Fatma, Z.H. (2017) Anxiety Effect in the Success Rate of Intrauterine Insemination (IUI) and *In Vitro* Fertilization (IVF). *Open Access Library Journal*, 4: e3691. <https://doi.org/10.4236/oalib.1103691>

**Received:** May 26, 2017

**Accepted:** June 20, 2017

**Published:** June 23, 2017

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## Abstract

**Background:** Infertility has a tendency to become potential physical and emotional stressors. The current progressive advances in fertility technology have encouraged more infertile couples to seek for the cause of infertility and take measures to improve their fertility. It is not uncommon that these couples experience emotional distress when they are undergoing fertility treatments. Although it is controversial, some experts argue that this emotional distress affects the success of fertility programs, such as intrauterine insemination and *in vitro* fertilization programs. **Objective:** The aim of the study was to investigate the relationship between successful pregnancy and anxiety in patients undergoing intrauterine insemination (IUI) and *in vitro* fertilization (IVF) programs. **Material and method:** A total of 39 patients undergoing intrauterine insemination and *in vitro* fertilization program in Aster clinic of Dr. Hasan Sadikin General Hospital during period of September-November 2016 were measured for their anxiety level using Zung Self-Rating Anxiety Scale. The results were then categorized as not anxious (score of 20 - 44) and anxious (45 - 80). Data were then compared against successful pregnancy after each program. **Results:** Of 39 patients, 23 underwent IUI and 16 underwent IVF. In the IUI group, 10 patients were not anxious (43.48%) and 13 people were anxious (56.52%) while in the IVF group 9 were not anxious (56.25%) and 7 were anxious (43.75%). Three patients (18%) who successfully conceived in the insemination program were those who were not anxious. Meanwhile, in the IVF group 3 patients (18.8%) also got pregnant with 2 of them were not anxious and 1 was anxious. A statistical calculation was performed using Fisher test, resulting in  $p = 0.068$  and  $p = 1.000$  for IUI and IVF, respectively. **Conclusion:** There is no significant correlation between the success of the fertility program and anxiety in patients undergoing IUI and

IVF programs.

## Subject Areas

Obstetrics and Gynecology

## Keywords

Anxiety, Intrauterine Insemination, *In Vitro* Fertilization, Pregnancy Rate

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## 1. Introduction

The inability to have children after being married for more than 1 year without using any contraception is commonly known as infertility. Infertility has increased over the past few decades and has become a social and challenging problem for healthcare providers around the world. More and more couples are coming to fertility centers because of difficulties to get pregnant. Advances in medical approaches have enabled us to continue looking for the causes of infertility and perform actions to improve fertility. As soon as the cause is known, the patient undergoes therapies to conceive. Treatments of infertility are divided into drugs, insemination and assisted reproductive technology (ART) [1]. It is not uncommon that the couple undergoing infertility therapies becomes susceptible to the problem of anxiety and stress associated with the experience of their infertility and the preparation of the infertility therapy [2], lack of enjoyment during intercourse, lack of respect for sexual intercourse, and even avoiding intercourse [3]. In fact, sometimes it is these problems that led to infertility as referred to by some authors as the “*psychogenic infertility*” that includes factors such as personality, family relationships, sexual disorders, guilty feelings, the urgent desire to have a baby, or fear of labor, which are all known to lower fertility [4]. Anxiety is the topic discussed in this study that is the most frequently found mental disorders [5]. The anxiety trait refers to individuals who tend to respond to stressful situations with increased anxiety. The state of anxiety is a subjective emotional condition that is temporarily or momentarily experienced by individuals due to tensions and anxiety, triggering the autonomic nervous system activities [6].

The assisted reproductive technology (ART) also contains risk factors that can cause behavioral and psychological changes for those who receive it. There are 3 main issues that are routinely experienced by patients during the couple’s preparation both before and during the therapy. First is the thought of the possibility of permanent infertility or losing hope of having children. Second is the expectation towards the outcome of therapy itself. The third is during the procedure, or what is referred to as procedural or situational distress in which anxiety may arise from fear of daily hormone injections or pain during oocyte retrieval or emotionally tense moment during the embryo transfer. In a recent study of couples undergoing ART, it is evident that these couples tend to have a high lev-

el of anxiety [7] [8] [9].

The importance of finding out the factors that can affect the success of fertility therapy is also a priority in the development of today's assisted reproductive technology. Attention is more focused on the negative consequences on the mental state as the consequences of infertility and the procedure even tends to be invasive. One of the issues examined in this type of research is anxiety. The effect of anxiety is one of the psychological factors that have been studied before. Frustration, aggression, depression, and anxiety are known to affect the success of pregnancy. Previous data on these effects conclude that high level of anxiety affects the number of cycles of insemination that must be endured by the patients to get pregnant and also the incidence of spontaneous abortion that occurs early in pregnancy, which is more probable in anxious pregnant women than in other pregnant women [10]. A study by Britt, *et al.* showed that a higher level of anxiety was more frequently found in infertile couples compared to other couples. They also concluded that during fertility therapies, many couples are relatively stressed [11].

Intrauterine insemination, a therapeutic process by placing washed spermatozoa transcervically into the uterine cavity becomes the first choice of infertile couples with mild causes, especially those cases with weak sperms, anovulation, endometriosis with at least 1 patent tube, and unexplained infertility. The reason why this procedure and ovulation induction is selected as the first choice includes the practicality because it is simple, low cost, and hardly leads to serious complications [12].

Assisted reproductive technologies such as *in vitro* fertilization and intracytoplasmic sperm injection are more complex and may lead to psychological impacts. In each cycle of *in vitro* fertilization, 9 to 12 days after injection are usually required stimulate oocyte production, oocyte removal via transvaginal ultrasonography, fertilization of the oocyte with partner sperm in the laboratory, and transfer the resulting embryo into the uterus. Then the couple has to wait 2 to 3 weeks to find out whether implantation or pregnancy occurs. The duration of each stage of *in vitro* fertilization can create psychological effects on the patient. Turner *et al.*, when researching 44 women, found an increase of anxiety of almost all women underwent *in vitro* fertilization therapy based on the psychometric results. He also found that women who initially had a low level of anxiety prior to oocyte retrieval have a higher rate of successful pregnancy [13]. On the contrary, some studies fail to prove the connection between anxiety and the success of fertility treatment [6] [14], including a meta-analysis of 31 prospective study. In this study, one of the findings is that no association is found between anxiety disorders and the therapeutic efficacy of the assisted reproductive therapy (ART) [15].

This study aimed to determine the relationship between the success of therapy and anxiety in patients undergoing intrauterine insemination (IUI) and *in vitro* fertilization (IVF) programs. These results of this study can be used as scientific evidence for the development of therapeutic and psychological therapies in im-

proving the success of reproductive technology in infertile women.

## 2. Methods

This study measured the level of anxiety in every patient receiving fertility treatment in Aster Fertility Clinic of Dr. Hasan Sadikin General Hospital Bandung during period of September-November 2016. The subjects of this study included women who underwent fertility therapies and had not declared to be pregnant. The inclusion criteria were patients/participants underwent intrauterine insemination and IVF programs that can be contacted either directly or via telephone. The exclusion criteria were patients/participants underwent other fertility programs in addition to intrauterine insemination and *in vitro* fertilization. Based on categorical comparative analysis test, minimal 15 samples are needed. Variables used in this study were patient characteristics and the effect of anxiety on the success of intrauterine insemination and IVF.

The state of anxiety was identified using Zung Self-Rating Anxiety Scale [16] which had been translated into Indonesian. The questionnaire containing 20 questions, with a range of scores of 1 to 4 per question, the resulting scores were interpreted as follows: 20 to 44 as normal/no anxiety, 45 - 59 as mild to moderate anxiety level, 60 - 74 as severe anxiety level, and 75 - 80 as extreme anxiety level. Patients were then interviewed after the therapy. In IUI patients, the pregnancy check was performed starting 2 weeks after insemination. In IVF patients, a pregnancy check is performed during the follow up visit to the clinic. The results were processed using a table by counting the number and percentage. Data were analyzed using Microsoft Excel and SPSS. The p value of <0.05 was considered statistically significant.

This study was approved by the hospital ethics committee. Any information collected from patients has been and will remain confidential. All the patients have agreed to sign the informed consent and have a whole understanding of this study.

## 3. Result

In this study, 39 subjects were recruited. The variables used are patient characteristics and effect of anxiety to the success of pregnancy. The subjects were divided into 2 separate groups: subjects underwent intrauterine insemination and subjects underwent *in vitro* fertilization.

The characteristics of intrauterine insemination and *in vitro* fertilization patients are presented in **Table 1** based on age, education, wife's occupation, husband's occupation, number of children, and infertility status. The age composition of patients underwent insemination were 14 patients were 35 years old (60.8%); 6 patients were 35 - 40 years old (26.1%) and 3 patients were 40 years old and above (13.0%). Meanwhile, the age composition for the age criteria for fertilization program patient is as follows: 7 patients were 35 years old (43.7%), 9 patients were 35 - 40 years old (56.3%), and none was over the age of 40 years old. Apparently the insemination program tends to be chosen by

**Table 1.** Characteristics of intrauterine insemination and *in vitro* fertilization patients in Aster Clinic of Dr. Hasan Sadikin General hospital Bandung.

Characteristics	Group	
	Insemination n (%)	<i>In Vitro</i> Fertilization n (%)
<b>Age</b>		
<35 yrs.	14 (60.8)	7 (43.7)
35 - 40 yrs.	6 (26.1)	9 (56.3)
>40 yrs.	3 (13.0)	0 (0)
<b>Education</b>		
Junior High School	0 (0)	1 (6.2)
Senior High School	8 (34.8)	4 (25)
D3	5 (21.7)	1 (6.2)
Bachelor	7 (30.4)	8 (50.0)
Master	3 (13.0)	2 (12.5)
<b>Wife's Occupation</b>		
Civil Servant	4 (17.4)	4 (25.0)
Private Employee	7 (30.4)	2 (12.5)
Housewife	7 (30.4)	4 (25.0)
Others	5 (21.7)	6 (37.5)
<b>Husband's Occupation</b>		
Civil Servant	5 (21.7)	2 (12.5)
Private Employee	8 (34.8)	6 (37.5)
Others	10 (43.4)	8 (50.0)
<b>Infertility Status</b>		
Primary	23 (100)	14 (87.5)
Secondary	0 (0)	2 (12.5)

younger infertile couples (under 35 years) whereas in *in vitro* fertilization was mostly chosen by those who were 35 - 40 years of age.

The data on educational level of the intrauterine insemination patients presented that 8 patients graduated from senior high school (34.8%), 5 graduated from D3 program (21.7%), 7 were bachelor program graduates (30.4%), and 3 had a master degree (13.0%). Meanwhile, the educational level of the *in vitro* fertilization patients showed that 1 patient graduated junior high school (6.2%), 4 graduated from senior high school (25.0%), 1 graduated from D3 program (6.2%), 8 graduated from bachelor program (50.0%) and 2 had a master degree (12.5%). It seems that the majority patients undergoing intrauterine insemination programs were senior high school graduate whereas most of the *in vitro* fertilization patients have graduated from a bachelor program. This level of education may have an effect on the selection and decision making on the choice of fertility therapy chosen by the couple.

In terms the job composition of the wives who underwent the intrauterine insemination program, the data show that 5 were civil servants (21.7%), 7 were

private employees (30.4%), 7 were housewives (30.4%), and 5 had other jobs (21.7%). Meanwhile, for the *in vitro* fertilization program, the job composition presented that 4 were civil servants (25.0%), 2 were private employees (12.5%), 4 were housewives (25.0%), and 6 had other jobs (37.5%). As for the husbands of patients who underwent intrauterine insemination program, 5 were civil servants (21.7%), 8 were private employees (34.8%), and 10 had other jobs (34.8%). For the husbands of the *in vitro* fertilization patients, 2 were civil servants (12.5%), 6 were private employees (37.5%), and 8 had other jobs (50.0%).

The infertility status of all intrauterine insemination patients was primary infertility ( $n = 23$ , 100%) while 14 of the *in vitro* fertilization patients experienced primary infertility (87.5%) with 2 had secondary infertility (12.5%).

**Table 2** describes anxiety in each type of fertility therapy. In intrauterine insemination, the majority of patients experienced anxiety (56.52%), whereas in *in vitro* fertilization, the majority of patients did not experience anxiety (56.25%). There is no significant difference in terms of anxiety by type of fertility therapy ( $p > 0.05$ )

In **Table 3**, the effect of anxiety on successful pregnancy in intrauterine insemination patients (**Table 3**) shows that there is no significant difference in terms of the relationship between anxiety status and the insemination therapy outcome ( $p = 0.068$ ).

In **Table 4**, the effect of anxiety on successful pregnancy in *in vitro* fertilization patients shows that there is no significant difference in terms of the relationship between anxiety status and the *in vitro* fertilization program outcome ( $p = 1.00$ ).

**Table 2.** Anxiety by type of fertility therapy in Aster Clinic of Dr. Hasan Sadikin General hospital Bandung.

Program	Normal/without anxiety n (%)	With anxiety n (%)	Total	
Intrauterine Insemination	10 (43.48)	13 (56.52)	23 (100)	Fisher Exact Test = 0.52 $p > 0.05$
<i>In Vitro</i> Fertilization	9 (56.25)	7 (43.75)	16 (100)	
Total	19 (48.72)	20 (51.28)	39 (100)	

**Table 3.** Effect of anxiety on the success of therapy in patients participating in intrauterine insemination.

		Insemination Therapy Outcome		Total	P value
		Pregnant n (%)	Not Pregnant n (%)		
Anxiety Status	Normal	3 (30)	7 (70.0)	10 (100.0)	0.068
	Anxious	0 (0.0)	13 (100.0)	13 (100.0)	
	Total	3 (18.0)	20 (87.0)	23 (100.0)	

**Table 4.** Effect of anxiety on the success of therapy in patients participating in *in vitro* fertilization program.

		<i>In Vitro</i> Fertilization Therapy Outcome		Total	P value
		Pregnant n (%)	Not Pregnant n (%)		
Anxiety Status	Normal	2 (22.2)	7 (77.8)	9 (100.0)	1.000
	Anxious	1 (14.3)	6 (85.7)	7 (100.0)	
	Total	3 (36.5)	13 (81.3)	16 (100.0)	

#### 4. Discussion

This study correlates the successful outcome in the form of pregnancy with the presence of anxiety in patients' undergoing intrauterine insemination and *in vitro* fertilization programs. From the results, it is evident that there is no significant association between the success of therapy and anxiety in patients undergoing intrauterine insemination and *in vitro* fertilization programs. Some studies from other researchers also do not see this relationship. A meta-analysis study by Boivin *et al.* that compared 14 studies with 3584 infertile women undergoing infertility treatment. Presented that anxiety or depression (emotional distress) is not the cause of the failure of fertility treatment [17].

Another study conducted by Hashemi *et al.* evaluated both the effect of state of anxiety and anxiety trait on the success rate of ART. At the end of his research, Hashemi *et al.* did not find any effect of state of anxiety and anxiety trait in pregnancy success [6].

Another study that supports the above research that there is no significant effect of ART therapy and the prevalence of anxiety disorders is a study on a woman group in Denmark that includes 98,320 women that shows no relationship in the success of the infertility treatment between those with and without the risk of anxiety [18]. A study by Milad *et al.* and Harlow *et al.* stated that both pregnant and non-pregnant groups have a similar anxiety levels. The high anxiety and stress also does not predict adverse pregnancy outcomes [19] [20]. It has been reported also that infertility patients undergoing fertility treatment sometimes suppress their feelings of stress and anxiety because they want to show to the clinic that they function well, both socially and psychologically [21].

There are several studies that show the effect of anxiety on the pregnancy success in patients undergoing intrauterine insemination and ART. Kokanali *et al.* concluded that the state of anxiety affects the success of intrauterine insemination, and they suggested the need for counseling program in intrauterine insemination therapy [22]. In another study performed by Matthiesen *et al.* a significant correlation was found between stress and distress and the reduced success of becoming pregnant in ART program [15]. Some researchers even learned the effect in the body when a woman experienced anxiety and its effect on the

therapy. Some studies found that existing anxiety and high cortisol level before oocyte retrieval (OR) and embryo transfer (ET) will lead to low number of successful pregnancy [23].

This study did not find a significant effect of anxiety on the success of getting pregnant in patients undergoing intrauterine insemination and *in vitro* fertilization programs. This may be due to the fact that Aster Fertility Clinic of Dr. Hasan Sadikin General Hospital Bandung, routinely conducts infertility classes for prospective participants of the fertility program so they know the steps of the therapy and issues regarding infertility. Patients also had discussion, sharing experience from those who have participated in a fertility program before. So it is likely that many potential patients of the fertility program have a relative mental readiness before undergoing the fertility therapy. This should be examined further in further research.

This study has a limitation in addition to the limited sample, which is the presence of some confounding factors that may affect the success of the program such as caffeine and alcohol intake and psychosocial factors such as the stress level of the husband. Biochemical markers of stress like cortisol were also not measured in this study. Hence, future studies are expected to be able to investigate the relationship between anxiety and the above risk factors that may affect patients during data collection of this study.

## 5. Conclusion

There is no significant relationship identified in this study between the success of getting pregnant and the presence of anxiety in patients who undergo intrauterine insemination and *in vitro* fertilization programs.

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