

Research Article

Emotional Impact of In Vitro Fertilization (IVF): Anxiety, Depression, and their Relationship with Pregnancy Outcomes

Feranindhya Agiananda^{1*}, Raden Muharram Natadisastra², Nurmiati Amir³, Irwanto⁴, Tiara Aninditha⁵, Sasanto Wibisono³, Tuti Wahmurti⁶, Aria Kekalih⁷, Artasya Karnasih³, Achmad Samjunanto⁸, Putri Air Puspaseruni³, Dyani Pitra Velyani⁸, Regina Prayangga³

¹Doctoral Program in Medical Sciences

²Department of Obstetrics and Gynecology

³Department of Psychiatry

Faculty of Medicine Universitas Indonesia,

Dr. Cipto Mangunkusumo General Hospital Jakarta

⁴Faculty of Psychology, Universitas Katolik Indonesia Atma Jaya, Jakarta

⁵Department of Neurology, Faculty of Medicine Universitas Indonesia

Dr. Cipto Mangunkusumo General Hospital, Jakarta

⁶Department of Psychiatry Faculty of Medicine Universitas Padjadjaran Bandung

⁷Department of Community Medicine Faculty of Medicine Universitas Indonesia Jakarta

⁸Department of Psychiatry Faculty of Medicine Universitas Trisakti Jakarta

Abstract

Objectives: To examine anxiety and depression experienced by women at different stages of IVF and to analyze their association with pregnancy outcomes.

Methods: This cohort study was conducted at Dr. Cipto Mangunkusumo General Hospital and Dr. Sander B. Daya Medika Clinic from May 2018 to March 2023. Data were collected using questionnaires and assessments during IVF, focusing on anxiety, depression, and pregnancy outcomes. Chi-square and Fisher's exact tests were used to assess associations between variables, while Friedman ANOVA was applied for longitudinal analysis of anxiety and depression scores across IVF stages.

Results: A total of 61 participants were included in the final analysis. Significant changes in anxiety and depression were observed throughout the IVF process. Both anxiety ($p < 0.001$, Kendall's $w = 0.19$) and depression ($p = 0.001$, Kendall's $w = 0.121$) levels increased significantly over time. A significant association was found between childbearing plans and anxiety ($p = 0.037$) at measurement II (before embryo transfer), as well as between education level and depression ($p = 0.038$) at measurement III (before pregnancy testing). However, no statistically significant association was observed between anxiety or depression scores and pregnancy outcomes across the three measurement points ($p > 0.05$).

Conclusion: Anxiety and depression significantly increase during IVF but are not associated with clinical pregnancy rates. These findings highlight the importance of mental health screening and psychiatric support during IVF to enhance women's comfort and help them navigate the process more effectively.

Keywords: anxiety, depression, in Vitro Fertilization (IVF), pregnancy outcomes, women.

Correspondence Author. Feranindhya Agiananda. Department of Psychiatry, Faculty of Medicine, Universitas Indonesia, Jakarta 10430, Indonesia. Email; feranindhya71@office.ui.ac.id, feranindhya@gmail.com. Mobile Phone: +628161696160

INTRODUCTION

Conception and reproduction serve as fundamental elements in the lives of many couples. Consequently, when a couple encounters difficulties in achieving spontaneous conception, both partners often experience profound sadness and disappointment. If conception does not occur after one year of consistent, unprotected intercourse, the couple is classified as experiencing infertility.¹ In 2021, the World Health Organization (WHO) indicated that the rate of infertility in high-income countries is 17.8%, whereas it is 16.5% in low and middle-income countries.² In Indonesia, it is estimated that between 10% and 15% of women aged 15 to 45 experience infertility, which equates to around four to six million couples affected by both primary and secondary infertility.³ This condition is a significant source of psychological stress, with anxiety and depression being the most prevalent psychological disorders among individuals facing infertility.¹

Couples experiencing infertility often explore various avenues to achieve pregnancy, engaging in multiple evaluations and treatments in their pursuit of favorable outcomes. When alternative techniques, such as insemination, do not produce successful results, assisted reproductive technology (ART) becomes a viable option. In vitro fertilization (IVF), commonly known as the "test-tube baby" procedure, is a form of ART utilized after other methods have proven ineffective. The Centers for Disease Control and Prevention (CDC) indicates that the live birth rate following embryo transfer stands at 49.0% for women aged under 35, whereas this rate declines to 24.1% for women over the age of 40.^{4,5} In Indonesia, 48.9% of women who participated in in vitro fertilization (IVF) were aged below 35 years. The success rates for pregnancies resulting from IVF procedures varied between 24.6% and 37.3%.⁶

Many couples with infertility who undergo Assisted Reproductive Technology (ART) are at an increased risk of developing psychiatric disorders. High financial burden and uncertain efficacy of these treatments can impose considerable pressure on couples engaged in IVF.⁷ Research indicates that various stages of in vitro fertilization (IVF), such as hormone stimulation, ovarian stimulation, oocyte retrieval, embryo transfer, and the ensuing waiting period for results, are particularly stressful for women undergoing these procedures.^{8,9} At the commencement of

treatment, women often express significant concerns regarding the number of injections they must endure, the dietary limitations required for optimal results, the expected physical discomfort, and most importantly, the probability of achieving a successful IVF cycle. During subsequent monitoring appointments, their apprehension centers on the advancement of their treatment. On the days designated for oocyte retrieval and embryo transfer, women experience anxiety related to the quality and quantity of the eggs and embryos, respectively. Many women have identified the two-week waiting period following embryo transfer, during which they await pregnancy results, as the most stressful phase of the entire process.¹⁰

The distinction in anxiety and depression levels among infertile couples at various stages of IVF and their correlation with assisted pregnancy outcomes have not been frequently examined. Previous studies indicate that the effectiveness of IVF may be influenced by psychological factors, including the level of distress experienced by women prior to and during treatment, but other studies find no association. Therefore, this study investigates anxiety and depression faced by women at different stages of IVF and analyzes their association with pregnancy outcomes.

METHODS

This study was designed as an analytical cohort study to assess the impact of IVF on the psychiatric aspects of women undergoing the treatment, particularly the presence of anxiety and depression. Data collection was conducted at Yasmin Infertility Clinic, Cipto Mangunkusumo General Hospital (RSCM), and Dr Sander B. Daya Medika Clinic from May 2018 to March 2023. This study was approved by the Ethics Committee of the Faculty of Medicine, Universitas Indonesia (ND308/UN2.F1/ETIK/PPM0002/2023).

The calculated target sample size was 100 participants including drop out of 20%. Women aged 25-42 years scheduled for IVF were eligible for participation. Exclusion criteria included individuals with psychotic disorders, severe anxiety, and severe depression. Participants were selected using non-probability, consecutive sampling, enrolling each eligible woman until the target sample size was achieved. Screening for severe mental disorders was conducted using the Mini-International Neuropsychiatric Interview (M.I.N.I.) instrument, a semi-structured interview

to diagnose mental disorder based on the diagnostic criteria of International Classification of Disease (ICD)-10. Each woman gave written consent prior to participating in the study.¹¹

Study data was collected using structured questionnaires at important time points throughout IVF; before the start of the treatment, before embryo transfer, and before pregnancy test. Demographic and gynecological information were obtained using questionnaires and the subjects' medical records at the initial stage of the study. Anxiety and depression symptoms, as the primary outcomes, were assessed using Hamilton Anxiety Rating Scale (HAM-A) and Hamilton Depression Rating Scale (HAM-D). Both instruments consist of semi-structured interviews conducted by a trained psychiatrist.

HAM-A, which contains 14 items, assesses anxiety severity through components including anxious mood, tension, fears, insomnia, difficulty in concentrating, and physical symptoms related to anxiety. The scale was translated and validated for the Indonesian population, achieving a Cronbach's alpha reliability coefficient of 0.756.¹² HAM-D, which comprises 17 items, evaluates the severity of depression based on components such as mood, feelings of guilt, suicidal ideation, insomnia, work performance and activities, psychomotor retardation or agitation, anxiety, somatic symptoms, and weight loss. This scale has undergone translation and validation for the Indonesian population, exhibiting a sensitivity and specificity of 93.3%.¹³ The semi-structured interviews were conducted by the same trained

psychiatrist to ensure consistency in scoring. Scores greater than or equal to 8 HAM-A and HAM-D were used to classify mild to moderate anxiety and depression, respectively, based on thresholds validated in previous studies for the Indonesian population. Pregnancy results were obtained from the medical record, evaluating urinary beta-hCG results approximately six weeks after recruitment as a part of IVF's routine procedure.

The data obtained was then subjected to analysis utilizing Statistical Package for the Social Sciences (SPSS) version 27. Participants who dropped out were excluded from the analysis. Categorical variables were analyzed using Chi-Square and Fisher's exact tests as appropriate, to examine associations between demographic, gynecological, anxiety, depression, and pregnancy outcome variables. For longitudinal analysis of anxiety and depression scores across the IVF, the Friedman ANOVA test was applied, followed by post hoc analysis with Bonferroni adjustment.

RESULTS

Out of 100 samples initially planned, 87 subject data were ultimately collected. Thirteen subjects were excluded for not meeting the inclusion criteria. Throughout the study, 26 subjects dropped out at various measurement stages, with most dropouts related to the IVF procedure. A total of 61 subjects completed the study (Figure 1).

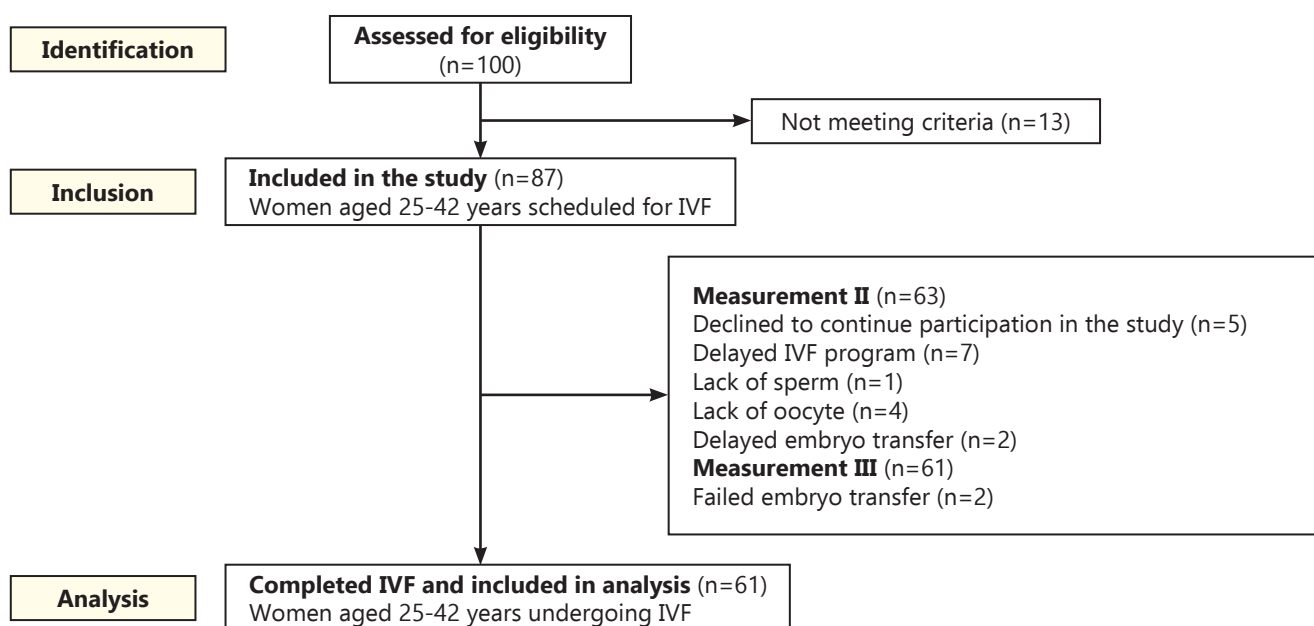


Figure 1. Flowchart of study design

Table 1 shows the distribution characteristics in research subjects at the initial stage of the study prior to the start of IVF. The majority of subjects was under 35 years (55.7%), having bachelor's or master's degree (90.2%), having been infertile for 5-10 years due to mixed etiology, planning to immediately have a child, and on their first cycle of IVF. At the beginning of the study, 42% of the subjects exhibited no anxiety or only minimal levels, while approximately 41% reported mild anxiety symptoms. Additionally, 52.5% of the participants experienced no depression or only minimal depressive symptoms.

Table 1. Subject Characteristics (n=61)

Characteristics	n	%
Demographic		
Age (y o)		
< 35	34	55
35-37	17	27.9
38-40	8	13.1
>40	2	
Education level		
Bachelor's master	55	90.2
Associate's	6	9.8
Gynecological		
Duration of Infertility (years)		31
< 5	19	50.8
5-10	31	18
> 10	11	
Childbearing Plan		88
Not delaying	54	11.5
DElaying	7	
Type of Infertility Experienced		
Female	18	29.5
Male	10	16.4
Mixed	33	54.1
Psychiatric		
Anxiety		
Not present or minimum	26	42.6
Mid	25	41.0
Moderate	10	16.4
Depression		
Not present or minimum	32	52.5
Mild	27	44.3
Moderate	2	3.3

Figure 2 illustrates the changes in anxiety scores among research subjects based on the HAM-A instrument. There was an increase in anxiety scores observed in Measurement II, conducted before the embryo transfer phase, which then tended to stabilize in Measurement III, conducted prior to the beta- hCG examination. A slightly different pattern was observed in depression scores among research subjects based on the

HAM-D instrument (Figure 3), which showed an increase in Measurement II and a further rise in Measurement III.

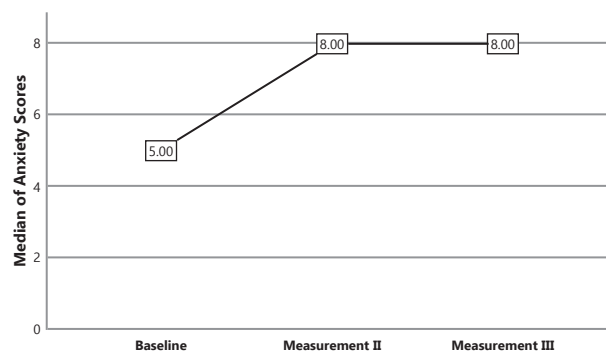


Figure 2. Anxiety Levels throughout IVF based on the Hamilton Anxiety Rating Scale (HAM-A)

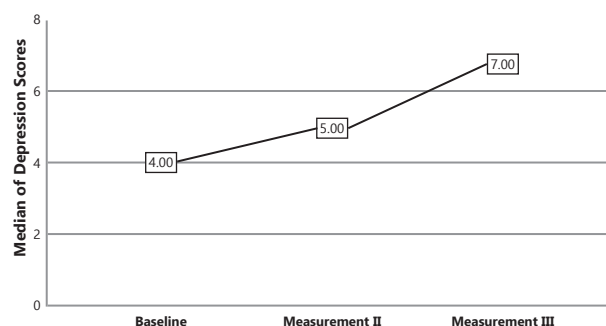


Figure 3. Depression Levels throughout IVF based on the Hamilton Depression Rating Scale (HAM-D)

The study revealed significant changes in anxiety and depression throughout IVF. Anxiety levels, as measured by the HAM-A scale, showed a significant rise across the IVF timeline ($p < 0.001$, Kendall's $w = 0.19$). The HAM-A scores rose markedly from a median of 5.00 (range: 0.00–18.00) at baseline to 8.00 (range: 0.00–20.00) before embryo transfer, maintaining this level until before the pregnancy test ($p < 0.001$). Similarly, depression levels, captured using the HAM-D scale increased from a median of 4.00 (range: 0.00–16.00) at baseline to 5.00 (range: 0.00–15.00) before embryo transfer and reaching 7.00 (range: 0.00–16.00) before the pregnancy test ($p = 0.001$, Kendall's $w = 0.121$).

Anxiety and depression scores showed a significant increase over time, as indicated by the Friedman ANOVA test. The median anxiety score rose from 5.00 at baseline to 8.00 at both Measurement II and III ($p < 0.001$), with a Kendall's W of 0.19, suggesting a moderate effect size. Similarly, depression scores increased from a median of 4.00 at baseline to 5.00 and 7.00 in subsequent measurements ($p = 0.001$), with a Kendall's W of 0.121, indicating a weaker but still meaningful trend.

These findings suggest a consistent upward shift in both anxiety and depression levels across the three time points, with statistically significant changes and modest agreement in rank ordering.

The analysis revealed significant changes in anxiety and depression scores over time. Anxiety scores showed a moderate correlation ($r = 0.50$) between baseline and both Measurement II and III, with highly significant p -values (< 0.001), indicating a notable increase in anxiety symptoms. However, no change was observed between Measurement II and III ($r = 0.00$, $p = 1.00$), suggesting a plateau in anxiety levels.

Similarly, depression scores increased significantly from baseline to Measurement II ($r = 0.34$, $p = 0.026$) and to Measurement III ($r = 0.45$, $p = 0.001$), reflecting a progressive rise in depressive symptoms. Yet, the difference between Measurement II and III was not significant ($r = 0.11$, $p = 1.000$), indicating stabilization in depression levels after the initial increase.

Post hoc analyses confirmed significant increases in both anxiety and depression during

the course of IVF. It showed significant increases in anxiety levels from baseline to both before embryo transfer ($r = 0.50$, adjusted $p < 0.001$) and prior to the pregnancy test ($r = 0.50$, adjusted $p < 0.001$). The lack of a significant difference between the two latter measurements ($p = 1.00$) suggests sustained anxiety throughout the latter stages of the IVF process. This pattern highlights the potentially stress-inducing impact of certain important points during IVF and the necessity for targeted psychological support during these phases.

Post hoc analyses also revealed a statistically significant rise in depression levels from baseline to both subsequent measurements ($r = 0.34$, adjusted $p = 0.026$ and $r = 0.45$, adjusted $p = 0.001$, respectively). However, no significant difference was observed between scores before embryo transfer and before the pregnancy test (adjusted $p = 1.00$). This suggests a cumulative burden of emotional distress during the IVF cycle, potentially linked to hormonal influences, treatment expectations, and procedural stress.

Table 2. Association between Subject Characteristics and Anxiety Levels (n=61)

Characteristics		Anxiety								
		Baseline ^a		P-value	Measurement II ^a		P-value	Measurement III ^a		P-value
		No-Minimal Anxiety	Mild-Moderate Anxiety		No-Minimal Anxiety	Mild-Moderate Anxiety		No-Minimal Anxiety	Mild-Moderate Anxiety	
Demographic										
Age	< 35	25 (61.0)	9 (45.0)	0.238 ^c	17 (63.0)	17 (50.0)	0.311 ^c	14 (58.3)	20 (54.1)	0.742 ^c
	≥ 35	16 (39.0)	11 (55.0)		10 (37.0)	17 (50.0)		10 (41.7)	17 (45.9)	
Education Level	Bachelor's or master's degree	37 (60.7)	18 (29.5)	1.000 ^f	25 (41.0)	30 (49.2)	0.685 ^f	23 (37.7)	32 (52.5)	0.388 ^f
	Associate's degree	4 (6.6)	2 (3.3)		2 (3.3)	4 (6.6)		1 (1.6)	5 (8.2)	
Gynecological										
Duration of Infertility	< 5	14 (34.1)	5 (25.0)	0.586 ^f	7 (25.9)	12 (35.3)	0.542 ^f	8 (33.3)	11 (29.7)	0.691 ^f
	5-10	21 (51.2)	10 (50.0)		16 (59.3)	15 (44.1)		13 (54.2)	18 (48.6)	
	> 10	6 (14.6)	5 (25.0)		4 (14.8)	7 (20.6)		3 (12.5)	8 (21.6)	
Childbearing Plan	Not delaying	35 (85.4)	19 (95.0)	0.409 ^f	21 (77.8)	33 (97.1)	0.037 ^f	20 (83.3)	34 (91.9)	0.418 ^f
	Delaying	6 (85.7)	1 (5.0)		6 (22.2)	1 (2.9)		4 (16.7)	3 (8.1)	
Type of Infertility	Female	14 (34.1)	4 (20.0)	0.512 ^c	8 (29.6)	10 (29.4)	0.914 ^c	9 (37.5)	9 (24.3)	0.292 ^c
Experienced	Male	6 (14.6)	4 (20.0)		5 (18.5)	5 (14.7)		5 (20.8)	5 (13.5)	
	Mixed	21 (51.2)	12 (60.0)		14 (51.9)	19 (55.9)		10 (41.7)	23 (62.2)	

a = Count (percentage); C = Chi-Square test; F = Fisher's Exact Test; * p value < 0.05

Table 3. Association between Subject Characteristics and Depression (n=61)

Characteristics		Depression								
		Baseline ^a		P-value	Measurement II ^a		P-value	Measurement III ^a		P-value
		No-Minimal Depression	Mild-Moderate Depression		No-Minimal Depression	Mild-Moderate Depression		No-Minimal Depression	Mild-Moderate Depression	
Demographic										
Age	< 35	29 (56.9)	5 (50.0)	0.738 ^F	25 (56.8)	9 (52.9)	0.785 ^C	21 (58.3)	13 (52.0)	0.624 ^C
	≥ 35	22 (43.1)	5 (50.0)		19 (43.2)	8 (47.1)		15 (41.7)	12 (48.0)	
Education Level	Bachelor's or master's	46 (90.2)	9 (90.0)	1.000 ^F	39 (88.6)	16 (94.1)	1.000 ^F	35 (97.2)	20 (80.0)	0.038 ^F
	Associate's	5 (9.8%)	1 (10.0)		5 (11.4)	1 (5.9)		1 (2.8)	5 (20.0)	
Gynecological										
Duration of Infertility	< 5	17 (33.3)	2 (20.0)	0.117 ^F	14 (31.8)	5 (29.4)	0.977 ^C	12 (33.3)	7 (28.0)	0.888 ^C
	5-10	23 (45.1)	8 (80.0)		22 (50.0)	9 (52.9)		18 (50.0)	13 (52.0)	
	> 10	11 (21.6)	0 (0.0)		8 (18.2)	3 (17.6)		6 (16.7)	5 (20.0)	
Childbearing Plan	Not delaying	44 (86.3)	10 (100)	0.587 ^F	37 (84.1)	17 (100.0)	0.175 ^F	30 (83.3)	24 (96.0)	0.223 ^F
	Delaying	7 (13.7)	0 (0.0)		7 (15.9)	0 (0.0)		6 (16.7)	1 (4.0)	
Type of Infertility	Female	15 (29.4)	3 (30.0)	0.900 ^F	13 (29.5)	5 (29.4)	0.206 ^C	13 (36.1)	5 (20.0)	0.385 ^C
Experienced	Male	8 (15.7)	2 (20.0)		5 (11.4)	5 (29.4)		5 (13.9)	5 (20.0)	
	Mixed	28 (54.9)	5 (50.0)		26 (59.1)	7 (41.2)		18 (50.0)	15 (60)	

a = Count (percentage); C = Chi-Square test; F = Fisher's Exact Test; *p value < 0.05

The association between subject characteristics and anxiety (Table 2) and depression (Table 3) levels during IVF showed no statistically significant relationships across all measurements. Demographic factors such as age and education level were not significantly associated with anxiety or depression at baseline, second, or third measurements ($p > 0.05$ for all comparisons). Gynecological factors, including duration of infertility, childbearing plans, and type of infertility, similarly demonstrated no significant influence on anxiety or depression levels at any time point ($p > 0.05$).

The only notable finding was a marginal association between education level and depression at the third measurement, where women with higher education appeared less likely to report mild-to-moderate depression compared to those with lower education ($p = 0.038$). Another minor association was also found between childbearing plan and anxiety in the second measurement, showing that women who delay their pregnancy are less likely to be anxious ($p = 0.037$). However, this association was not consistently observed across earlier measurements. Overall, neither demographic nor gynecological characteristics emerged as consistent predictors of anxiety or depression levels in this cohort.

There were no statistically significant differences in psychiatric symptoms specifically anxiety and depression between pregnant and

non-pregnant women across three measurement points. At baseline, mild to moderate anxiety was reported in 36.1% of pregnant women and 28.0% of non-pregnant women ($p = 0.507$), with similar patterns observed in subsequent measurements (p -values: 0.973 and 0.656). Depression levels followed a comparable trend, with mild to moderate symptoms increasing slightly over time but remaining statistically insignificant between groups (baseline $p = 0.727$; Measurement II $p = 0.985$; Measurement III $p = 0.896$).

Overall, both groups experienced fluctuations in anxiety and depression levels, yet the differences were not significant. This suggests that pregnancy status did not play a decisive role in influencing the severity of psychiatric symptoms within the observed sample.

These findings support earlier results showing that anxiety and depression symptoms increased over time during the IVF process, but were not influenced by pregnancy status or linked to pregnancy outcomes. Psychological distress appeared to rise regardless of clinical results, highlighting the need for emotional support throughout treatment.

DISCUSSION

study, conducted at a tertiary hospital in Indonesia, is the first in the country to explore the impact of different stages of IVF on anxiety and depression levels in women undergoing

the treatment, as well as their relationship with pregnancy outcomes. The baseline characteristics observed in our sample largely align with those reported in other studies, supporting the generalizability of our findings. More than half of the research subjects were under 35 years old (55.7%), followed by those aged 35-37 years (27.9%), closely reflecting the demographic profile reported by the Indonesian Association for In Vitro Fertilization, which found that 50.07% of women undergoing IVF in Indonesia were under 35 years and 20.55% were aged 35-37 years.¹⁴

Furthermore, the majority of participants in our study had bachelor's or master's degree (90.2%), which aligns with the results of prior studies.¹⁵ Mixed infertility was the most common type observed in subject, aligning with the Indonesian Association for In Vitro Fertilization report, which identified mixed infertility in 40.22% of cases, followed by female infertility at 30.1% and male infertility at 22.71%.¹⁴ However, a notable difference in infertility duration was observed, with the majority of participants experiencing infertility for five to ten years. In contrast, previous research reported a typical infertility duration that aligned with marriage lengths of 1.5 to 6.2 years.¹⁶ This discrepancy may be partly attributed to the lack of IVF coverage under Indonesia's national health insurance, unlike in some developed countries. Cultural and socioeconomic influences may contribute significantly, as prior research has identified enduring myths, misinformation, and adverse perceptions regarding IVF within certain segments of the Indonesian population.¹⁷ These barriers may delay couples' pursuit of IVF, leading them to consider alternative treatments or save for the procedure due to its substantial cost.

At the beginning of the study, participants were at minimal levels of anxiety and depression, aligning with the results of prior studies that indicated anxiety and depression rates of 13.5% and 9.4%, respectively, among infertile couples before IVF.¹⁸ Other previous research has indicated that the majority of women participating in IVF reported experiencing predominantly mild levels of anxiety and depression.¹⁹ Based on demographic and gynecological characteristics, we found that the incidence of anxiety in measurement II (before embryo transfer) is related to childbearing plan. We also found that the depression in measurement III (before pregnancy test) is related to education level, but this association was not consistently observed

across earlier measurements.

Anxiety and Depression Levels throughout IVF

IVF is a final-line reproductive method for addressing infertility issues in couples. The high cost of IVF, the extensive stages involved, and the often-uncertain outcomes make the experience emotionally taxing, with many women describing the journey as an "emotional roller coaster." Women may experience symptoms of anxiety or depression that can impact their adaptability and the success of IVF.²⁰ In a previous study that involved 42000 women in Denmark, 35% were screened positive for depression before starting IVF.²¹ Another study conducted in 5 fertility practices in California found depression in 56.5% and anxiety in 75.9% of the women seeking infertility treatment.²²

The results of this study revealed significant changes in anxiety and depression throughout IVF. Anxiety levels, as measured by the HAM-A scale, showed a significant rise across the IVF timeline ($p < 0.001$, Kendall's $w = 0.19$). Depression levels, as measured by the HAM-D scale, also showed a significant rise across the IVF timeline ($p = 0.001$, Kendall's $w = 0.121$). This pattern is consistent with the findings of prior research, which indicated that anxiety levels in women undergoing IVF typically rise before and after embryo transfer (the period awaiting pregnancy test results), often attributed to heightened emotional responses during this time.²⁰ The incidence of depression is also noted to vary during the IVF process; however, it exhibits a slight distinction, as prior research has shown that peak levels of depression are typically observed immediately prior to the commencement of the IVF cycle.¹⁹

These findings are supported by post hoc analysis, which revealed significant increases in both anxiety and depression during IVF. The findings of this study are consistent with earlier research, which also identified a comparable trend in the fluctuations of anxiety and depression during the various phases of in Vitro Fertilization (IVF).¹⁹ Prior to embryo transfer, women tend to harbor elevated expectations regarding the success of IVF and exhibit apprehension regarding the oocyte retrieval procedure, particularly when performed without general anesthesia, which can exacerbate fears of pain and induce anxiety. Following embryo transfer, patients express concerns related to

the investment of time and financial resources, the efficacy of their psychological efforts, and the potential implications of a failed outcome. A prior investigation similarly found that women undergoing IVF experience the highest levels of anxiety post-embryo transfer, corroborating the results of this study, which indicates a sustained state of anxiety from the period preceding embryo transfer until the pregnancy test is conducted.²³

Association between Anxiety, Depression and Pregnancy Outcomes

The results of this study indicate that there was no association between anxiety and depression scores and pregnancy outcomes across the three measurement points during IVF. Previous research has yielded comparable results, indicating a lack of correlation between anxiety and depression and the rates of clinical pregnancy.²⁴ A study conducted in China found no significant differences between anxiety levels in women who obtained pregnancy in IVF and those who did not.²⁵ A similar study also found no association between the IVF outcome and psychological distress of women who did not obtain clinical pregnancy after their first embryo transfer.²⁶

The success of pregnancy through IVF can be attributed to a variety of factors, particularly those related to infertility. Conditions like obstructed fallopian tubes or male infertility can hinder the treatment process and diminish the likelihood of a successful outcome. Moreover, the quality of both oocytes and embryos, along with the thickness of the endometrium, plays a vital role in achieving successful fertilization and implantation. The presence of higher-quality oocytes and embryos markedly enhances the probability of conception. Additionally, numerous studies have underscored the significant impact of lifestyle choices on IVF success. Habits such as smoking, excessive alcohol intake, and obesity can adversely influence the effectiveness of IVF treatments.²⁷⁻³⁰

While anxiety and depression may not directly correlate with lower pregnancy rates, they can lead to diminished well-being after unsuccessful treatments. A prior investigation indicated an increase in both depression and anxiety in couples after IVF treatment failure.³¹ Another study found that infertile women with high levels of depression and anxiety symptoms had a lower quality of life following unsuccessful IVF treatment.³² Therefore,

psychosocial intervention and support should be provided effectively to reduce the psychological distress in these women.

Strengths and Limitations of the Study

Key strengths of this study include long-term monitoring throughout the IVF, enabling a clear observation of the increasing levels of depression and anxiety at each stage. However, there were limitations, one of which was this study is a prospective cohort study aimed at examining the levels of anxiety and depression in women undergoing IVF, without comparing them to a group receiving other infertility treatments. Therefore, the results cannot be definitively attributed solely to IVF, as they may also be influenced by other factors. A further constraint is the challenge associated with recruiting participants for the study. This study faced a relatively high dropout rate, which may have influenced the statistical power and generalizability of the findings. The dropouts can be attributed to several factors inherent to IVF, which is a dynamic procedure, and some participants experienced unexpected outcomes during the treatment, which indicated IVF failure even before the final pregnancy results could be assessed. As a result, these women were unable to continue with the treatment, and hence, could not complete the study.

In addition, this study does not include an evaluation of biological factors that may impact the IVF process and ultimately pregnancy outcomes, such as quality of the sperm, oocyte, embryo, and differences in individual hormone levels. Thus, future research ought to explore the adoption of more flexible data collection method, develop strategies aimed at maintaining participant engagement throughout the IVF journey, and take into account confounding variables that could affect the outcomes of IVF treatments.

CONCLUSION

Our findings demonstrate a significant increase in anxiety and depression throughout the stages of IVF, particularly before embryo transfer and while waiting for pregnancy test results. The foremost determinant affecting anxiety in measurement II (prior to embryo transfer) is childbearing plan, whereas the most critical factor linked to depression in measurement

III (before the pregnancy test) is the degree of educational attainment. Nonetheless, this correlation was not uniformly evident across all measurements and should be approached with caution in interpretation. These findings have important implications for clinical practice, as they underscore the necessity of mental health screening for all women undergoing IVF. Additionally, providing psychiatric support for women experiencing anxiety and depression during IVF is crucial to ensure their comfort and enable them to navigate the treatment more effectively.

ACKNOWLEDGEMENT

The authors wish to express appreciation and gratitude to all IVF patients who took part in this study for their contributions. We would also like to thank Prof. Ari Fahrial Syam, MD, the Dean of the Faculty of Medicine, Universitas Indonesia, Prof. Suhendro, MD, and Prof. Harrina Rahardjo, MD, from the Doctoral Program in Medical Science of the Faculty of Medicine, Universitas Indonesia, for their guidance and support. The authors would also like to thank the staff of the Department of Obstetrics and Gynecology and Department of Psychiatry in Dr. Cipto Mangunkusumo General Hospital, Yasmin Reproductive Cluster RSCM Kencana and Dr Sander B. Daya Medika Clinic, who have assisted in this research process.

CONFLICT of INTEREST

No competing interests were disclosed.

REFERENCES

1. Aimagambetova G, Issanov A, Terzic S, Bapayeva G, Ukybassova T, Baikoshkarova S, et al. The effect of psychological distress on IVF outcomes: Reality or speculations? *PLoS One*. 2020;15:1–14.
2. WHO World Health Organization. Infertility prevalence estimates. 2021: 55–94.
3. Harzif AK, Santawi VPA, Wijaya S. Discrepancy in perception of infertility and attitude towards treatment options: Indonesian urban and rural area. *Reprod Health*. 2019 Aug 19;16(1):126.
4. Carson SA, Kallen AN. Diagnosis and Management of Infertility: A Review. *JAMA*. 2021 Jul 6;326(1):65–76.
5. Centers for Disease Control and Prevention. 2021 Assisted Reproductive Technology Fertility Clinic and National Summary Report. US Dept of Health and Human Services. 2023.
6. Wiweko B, Mansyur E, Yuningsih T, Sini I, Silvana V, et al. Ten years of in vitro fertilization in Indonesia: Access to infertility care in a developing country. *Int J Gynaecol Obstet*. 2024 Jun;165(3):1144–50.
7. Liu YF, Fu Z, Chen SW, He XP, Fan LY. The Analysis of Anxiety and Depression in Different Stages of in vitro Fertilization-Embryo Transfer in Couples in China. *Neuropsychiatr Dis Treat*. 2021 Feb 25;17:649–57.
8. Miller N, Herzberger EH, Pasternak Y, Klement AH, Shavit T, Yaniv RT, Ghetler Y, Neumark E, Eisenberg MM, Berkovitz A, Shulman A, Wiser A. Does stress affect IVF outcomes? A prospective study of physiological and psychological stress in women undergoing IVF. *Reprod Biomed Online*. 2019 Jul;39(1):93–101.
9. Zannettoullis AT, Mastorakos G, Vakas P, Vlahos N, Valsamakis G. Effect of Stress on Each of the Stages of the IVF Procedure: A Systematic Review. *Int J Mol Sci*. 2024 Jan 5;25(2):726.
10. Awtani M, Kapoor GK, Kaur P, Saha J, Crasta D, Banker M. Anxiety and Stress at Different Stages of Treatment in Women Undergoing In vitro Fertilization-Intracytoplasmic Sperm Injection. *J Hum Reprod Sci*. 2019 Jan-Mar;12(1):47–52.
11. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiler E, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structural diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry*. 1998; 59 (suppl 20): 22–33.
12. Ramdan, I. M. Reliability and Validity Test of the Indonesian Version of the Hamilton Anxiety Rating Scale (HAM-A) to Measure Work-related Stress in Nursing. *J Ners*. 2019;14(1):33–40.
13. Driyana. The Proportion of Depression at Tegalrejo Community Health Center, Yogyakarta (Thesis). Yogyakarta. Universitas Gadjah Mada. 1989.
14. Wiweko B. Indonesian Association for In Vitro Fertilization's National Report 2020. 2020;1–47.
15. Mahalingaiah S, Berry KF, Hornstein MD, Cramer DW, Missmer SA. Does a woman's educational attainment influence in vitro fertilization outcomes? *Fertil Steril*. 2011 Jun 30;95(8):2618–20.
16. Ying L, Wu LH, Loke AY. Gender differences in emotional reactions to in vitro fertilization treatment: a systematic review. *J Assist Reprod Genet*. 2016 Feb;33(2):167–79.
17. Harzif AK, Santawi VPA, Wijaya S. Discrepancy in perception of infertility and attitude towards treatment options: Indonesian urban and rural area. *Reprod Health*. 2019 Aug 19;16(1):126.
18. Zhang, L., Shao, H., Huo, M. et al. Prevalence and associated risk factors for anxiety and depression in infertile couples of ART treatment: a cross-sectional study. *BMC Psychiatry*. 2022;22:616.
19. Liu YF, Fu Z, Chen SW, He XP, Fan LY. The analysis of anxiety and depression in different stages of in vitro fertilization-embryo transfer in couples in China. *Neuropsychiatr Dis Treat*. 2021;17:649–57.
20. Gabnai-Nagy E, Bugán A, Bodnár B, Papp G, Nagy BE. Association between Emotional State Changes in Infertile Couples and Outcome of Fertility Treatment. *Geburtshilfe Frauenheilkd*. 2020 Feb;80(2):200–210.
21. Sejbæk CS, Hageman I, Pinborg A, Hougaard CO, Schmidt L. Incidence of depression and influence of depression on the number of treatment cycles and births in a national cohort of 42,880 women treated with ART. *Hum Reprod*. 2013 Apr;28(4):1100–9.

22. Pasch LA, Holley SR, Bleil ME, Shehab D, Katz PP, Adler NE. Addressing the needs of fertility treatment patients and their partners: are they informed of and do they receive mental health services? *Fertil Steril*. 2016 Jul;106(1):209-215.e2.
23. Awtani M, Kapoor GK, Kaur P, Saha J, Crasta D, Banker M. Anxiety and stress at different stages of treatment in women undergoing in vitro fertilization-intracytoplasmic sperm injection. *J Hum Reprod Sci*. 2019;12(1):47-52.
24. Maroufizadeh S, Navid B, Omani-Samani R, Amini P. The effects of depression, anxiety and stress symptoms on the clinical pregnancy rate in women undergoing IVF treatment. *BMC Res Notes*. 2019 May 9;12(1):256.
25. Cui Y, Yu H, Meng F, Liu J, Yang F. Prospective study of pregnancy outcome between perceived stress and stress-related hormones. *J Obstet Gynaecol Res*. 2020 Aug;46(8):1355-63.
26. Peng M, Wen M, Jiang T, Jiang Y, Lv H, Chen T, et al. Stress, anxiety, and depression in infertile couples are not associated with a first IVF or ICSI treatment outcome. *BMC Pregnancy Childbirth*. 2021;21(1):1-8.
27. Dabbagh Rezaeiyyeh R, Mehrara A, Mohammad Ali Pour A, Fallahi J, Forouhari S. Impact of Various Parameters as Predictors of The Success Rate of In Vitro Fertilization. *Int J Fertil Steril*. 2022 Apr;16(2):76-84.
28. Amini P, Ramezanali F, Parchehbaf-Kashani M, Maroufizadeh S, Omani-Samani R, Ghaheri A. Factors Associated with In Vitro Fertilization Live Birth Outcome: A Comparison of Different Classification Methods. *Int J Fertil Steril*. 2021 Apr;15(2):128-34.
29. Wiweko B, Hestiantoro A, Sumapraja K, Muharam R, Andriyana H, Febia E, et al. Predictive Factors for Pregnancy in IVF: An Analysis of 348 Cycles. *Indones J Obs Gynecol*. 2010;34(4):180-4.
30. Wiweko B, Hestiantoro A, Natadisastra M, Sumapradja K, Mansyur E, Febia E. Not only embryo quality but also Endometrial Thickness Contributes to IVF outcome: a retrospective study of all IVF cycles in Yasmin Clinic, Jakarta, Indonesia. *Endometrial Thick Contrib to IVF outcome*. 2010;34(1):39-42.
31. Milazzo A, Mnatzaganian G, Elshaug AG, Hemphill SA, Hiller JE; Astute Health Study Group. Depression and anxiety outcomes associated with failed assisted reproductive technologies: A systematic review and meta-analysis. *PLoS One*. 2016 Nov 11;11(11):e0165.
32. Omani-Samani R, Ghaheri A, Navid B, Sepidarkish M, Maroufizadeh S. Prevalence of generalized anxiety disorder and its related factors among infertile patients in Iran: a cross-sectional study. *Health Qual Life Outcomes*. 2018;16(1):129.