

Factors attributed to depressive symptoms in women coping with infertility during the pandemic of COVID-19



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ABSTRACT

Background: The dissemination of coronavirus disease (COVID-19) has led to delayed infertility treatment and fear of contracting the virus which can affect the mental status of women with infertility. This research aimed to investigate whether fear, depression, perceptions, and knowledge related to COVID-19 affected infertility patients in seeking treatment and analyzed factors associated with depression during COVID-19 pandemic.

Method: This is a cross-sectional study utilizing an electronic survey distributed to infertility patients attending fertility services between May and July 2021. The primary outcomes were demographic characteristics, clinical parameters of infertility, depressive symptoms based on the Patient Health Questionnaire-9 (PHQ-9) score, and fear of COVID-19 scale (FCV-1 and FCV-2).

Results: A total of 533 patients were included. The fear of infertility treatment suspension due to COVID-19 was perceived by 34.1% of patients. The mean Patient Health Questionnaire-9 (PHQ-9) score was 4.55 ± 4.248 , with mild depression occurring in 33.4% of patients. Low income, delayed treatment, and fear of COVID-19 scale (FCV-1) score together could significantly predict depression status. Despite the pandemic, 94.7% of patients decided to continue the treatment.

Conclusion: The COVID-19 pandemic has given rise to stressors that may aggravate the psychological condition of women with infertility. However, the enthusiasm to continue the treatment remains undisturbed. It is imperative to offer emotional support and address the consequences of COVID-19 infection in women with infertility during the pandemic era.

Keywords: Infertility, COVID-19, depression, fear, PHQ-9.

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INTRODUCTION

severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been identified as the cause of coronavirus disease 2019 (COVID-19), with one of the significant consequences being severe respiratory tract illness. In March-April 2020, the American Society for Reproductive Medicine (ASRM) and the European Society of Human Reproduction and Embryology (ESHRE) responded to the pandemic with some key recommendations. The recommendations include: suspending the instigation of new treatment cycles to reduce the risk of vertical transmission and complications of COVID-19, mitigating complications from assisted reproductive treatments and pregnancy, supporting the shift in the utilization of health resources, and implementing social distancing policies.^{1,2} Nevertheless, these recommendations

could be deemed overly cautious in the early pandemic era, when little was known concerning the consequences of SARS CoV-2 infection on pregnancy and infants. These recommendations led to the suspension of fertility services. Due to a lack of knowledge surrounding the consequences of COVID-19, the delays in fertility treatments span several months, which may have significant impacts on the live birth rate, particularly in older female patients. One study in the United States found a decrease in the live birth rate in 369 women due to a delay in infertility therapy for one month.³ However, another research found no difference in live birth rates between women with a diminished ovarian reserve (anti-mullerian hormone [AMH] < 1.1 ng/ml) who started in vitro fertilization (IVF) cycles after 180 days from their initial consultation and women who started cycles after 90 days. Similar findings were found in women at the greatest risk for a poor response

to ovarian stimulation (women with AMH <0.5 ng/ml or aged more than 40 years old with AMH <1.1 ng/ml). Pregnancy rate between patients on immediate and delayed therapy who had diminished ovarian reserve was also comparable.⁴

This situation would be exacerbated by the fact that COVID-19 may significantly influence the economic sector.⁵ Economic stagnation may cause financial constraints for some patients; thus they have no choice but to suspend assisted reproductive technology (ART). Infertility is a problematic issue because females have significant pressure to bear children.⁶ Moreover, health insurance in some countries does not cover the cost of infertility treatment.⁷ Patients with middle to low income are more likely to present at an older age due to the need to save money before joining the program.

The fear of contracting the virus, economic problems, and the enforcement of large-scale restrictions may exacerbate anxiety and depression in infertility patients during the COVID-19 pandemic. The COVID-19 anxiety score was higher in patients who agreed with the infertility treatment delay policy compared to those who disagreed. Prevention of transmission, utilization of the healthcare system to deal with the pandemic, and the possibility of infection from mother to baby have caused patients to agree to postpone infertility therapy during the COVID-19 pandemic.⁸ However, it is unclear whether there is a relationship between fear during the COVID-19 pandemic and the incidence of depression in infertility women. We aimed to understand the factors attributed to depression symptoms in infertility patients during the COVID-19 pandemic and further determine whether fear, depression, and perception related to COVID-19 infection affected the patients' decisions to seek and continue treatment.

METHODS

Study participants and methodology

The research was conducted at infertility clinics in Jakarta, Indonesia, between May and July 2021. As a part of study recruitment, an anonymous electronic survey on the Google forms web application was sent to eligible couples via email and WhatsApp. The online

survey was distributed to 700 patients who had medical records at the infertility center in Jakarta at the time of the study. We included all infertility patients who were at the stage of infertility workup or treatment, aged between 20 and 44 years, and were willing to fill out the Google forms. A brief introduction was given to all participants explaining the purpose of this survey, and all necessary information was provided. The respondents voluntarily gave informed consent to participate in this study. Responses were anonymous, with no identifying details. The demographic characteristics of the subjects consisted of age, education level, occupation, family income, domicile, religion, and ethnicity. Infertility information covered the cause and duration of infertility, treatment programme required, history of ART failure, delay of infertility treatment due to the COVID-19 pandemic, and willingness to continue the program.

We implemented statements related to the probable consequences of COVID-19 infection on pregnancy to determine whether the COVID-19 outbreak impacted the patient's willingness to conceive. We evaluated the questions using a 5-point Likert scale from "strongly disagree" to "strongly agree". The questionnaire was composed of three different sections. The first part determined the presence of anxiety and fear related to the COVID-19 pandemic, the second part evaluated the Patient Health Questionnaire-9 (PHQ-9), and the third part evaluated the perceptions of the study subjects toward COVID-19 infections. We assessed the fear related to COVID-19 using the modified questionnaire utilized in the Iranian,⁹ and Turkish population,¹⁰ which is the FCV-19S scale. We added some questions related to pregnancy and infertility workup during the pandemic. In this study, FCV-1 was composed of general questions related to fear and anxiety of COVID-19 infections. While FCV-2 contained specific questions regarding infertility and future pregnancy during the pandemic.

The questionnaire had been validated with a Cronbach's alpha of 0.737. We reviewed the level of depression by using standardized and validated PHQ-9. The PHQ-9 is a questionnaire designed to screen for depression in primary care and

other medical settings. The questionnaire was assessed using a 4-point Likert scale from "never" to "almost always". The response for each question was scored 0 (never), 1 (several days), 3 (more than half the days), and 4 (nearly every day). The lowest and highest scores were 0 and 27, respectively. PHQ-9 scores of 5, 10, 15, and 20 exemplified mild, moderate, moderately severe, and severe depression, respectively.¹¹ The lowest score suggests low levels of depression, and the highest score signifies severe depression.

Ethics approval

This study was approved by the Faculty of Medicine, Universitas Indonesia Ethics Committee with the reference number: KET-1464/UN2.F1/ETIK/PPM.00.02/2020. Informed consent was obtained from all participants through the Google form with a statement that all data would be confidential. All methods were carried out under the ethical standards of the institutional research committee and conducted according to the Declaration of Helsinki. All methods were performed based on the relevant guidelines and regulations.

Data collection

Data were collected using the questionnaire previously mentioned. The data collected included the fear of COVID-19, anxiety-related COVID-19 infections, PHQ-9 and perceptions of COVID-19 infections.

Data analysis

Statistical analysis was conducted using SPSS version 22 (Statistical Package for the Social Sciences, version 22, SPSS Inc., Chicago, Illinois, USA). Data with normal distribution were presented as mean \pm standard deviation and skewed data as median and range. The qualitative data were analyzed by Chi-square or Fisher exact test as appropriate. The normally distributed continuous data were analyzed using the Pearson test. The not normally distributed data was analyzed using Spearman's rank correlation test. As appropriate, the comparison between groups was tested using the student t-test or Mann-Whitney U test. Multivariate regression analysis included determinant variables with univariate p-value <0.25. A

p-value of less than 0.05 was considered significant. Backward elimination was used.

RESULTS

Subject and study variables characteristics

Of 700 infertility patients, 533 patients with primary infertility completed the Google forms and were included in the analysis. The median age of the subjects was 31 years old (21-50 years old), with 73.0% being less than 35 years old. The most prevalent education level of the respondents was undergraduate (74.9%). Around 75.4% of subjects had an occupation, with 43.3% working as private employees and 24.6% unemployed. In addition, most of the subjects had an income of 357-714 USD per month (36.0%), with 62.9% living in rural areas.

The association between patients' characteristics and PHQ-9 score

We used validated PHQ-9 to screen for the possibility of major depressive disorder (MDD) among infertility patients during the COVID-19 pandemic. The mean PHQ-9 score of all patients was 4.55 ± 4.25 . There were 235 patients (44.1%) who suffered from depression, with mild depression being the most common (33.4%), followed by moderate (8.1%), moderately severe (1.5%), and severe depression (1.1%). We analyzed whether the socio-demographic characteristics of the patients impacted the risk of suffering from major depressive disorders. There was a significant difference in depressive status between patients of different ages, education levels, occupations, and incomes ($p < 0.05$). We found that the median PHQ-9 score was significantly higher in subjects under the age of 35 years (4.0 (0-27)), elementary school as the highest level of education (8.0 (6-10)), and an income of less than 357 USD per month (5.0 (0-21)). Based on occupation, the median PHQ-9 score was significantly higher in private workers (4.0 (0-24)), teachers (4.0 (0-17)), and unemployed (4.0 (0-15)). Religion, ethnicity, and domicile did not affect the PHQ-9 score ($p > 0.05$) (Table 1).

Table 1. Socio demographic characteristic of the subjects in accordance with PHQ-9 score.

Variables	n (%)	PHQ-9 Median (min-max)	p
Age			0.002 [†]
<35 years	389 (73.0)	4.0 (0-27)	
≥35 years	144 (27.0)	3.0 (0-24)	
Education level			0.015 [†]
Elementary school	2 (4.0)	8.0 (6-10)	
Secondary school	30 (5.6)	4.0 (0-16)	
Undergraduate	399 (74.9)	4.0 (0-27)	
Postgraduate	102 (19.1)	3.0 (0-18)	
Occupation			0.001 [†]
Private employee	231 (43.3)	4.0 (0-24)	
Government employee	73 (13.7)	3.0 (0-27)	
Health professional	59 (11.1)	2.0 (0-20)	
Teacher	39 (7.3)	4.0 (0-17)	
Unemployed	131 (24.6)	4.0 (0-15)	
Income (per month)			0.000 [†]
≤ 357 USD	160 (30.0)	5.0 (0-21)	
357-714 USD	192 (36.0)	4.0 (0-27)	
715-1071 USD	73 (13.7)	3.0 (0-21)	
1072-1428 USD	43 (8.1)	4.0 (0-12)	
≥1428 USD	65 (12.2)	2.0 (0-24)	
Domicile			0.130 [†]
Rural	335 (62.9)	4.0 (0-27)	
Urban	198 (37.1)	3.0 (0-17)	
Religion			0.655 [†]
Islam	429 (80.5)	4.0 (0-27)	
Catholic	28 (5.3)	3.0 (0-21)	
Protestant	57 (10.7)	3.0 (0-17)	
Hinduism	6 (1.1)	3.0 (0-13)	
Buddhism	13 (2.4)	4.0 (0-10)	
Ethnic group			0.460 [†]
Javanese	303 (56.8)	4.0 (0-27)	
Sumatran	162 (30.4)	3.0 (0-21)	
Sulawesi	9 (1.7)	1.0 (0-7)	
Kalimantan	4 (0.8)	3.0 (2-12)	
Balinese	5 (0.9)	1.0 (0-6)	
Chinese	31 (5.8)	4.0 (0-17)	
Others	19 (3.6)	4.0 (0-13)	

[†]Mann-Whitney U test

[†]Kruskal-Wallis test

The association between PHQ-9 scores and clinical parameters

Based on the clinical parameters of infertility, we found that the most common cause was unexplained (35.1%). Some patients had fertility therapy for less than 12 months (63.8%). Patients' median duration of infertility was five years (1-19 years). There was no statistically significant difference between the PHQ-9 scores and

the duration of infertility ($p > 0.05$). More than 50% of patients underwent an ART cycle (61.2%). There was a significant difference in the median and range of PHQ-9 scores between the group with delayed and not delayed treatment (4.0 (0-21)) due to COVID-19 versus not delayed (4.0 (0-27)) ($p < 0.05$). Despite this delay, almost all patients still desired to renew treatments (94.7%) (Table 2).

Table 2. The comparison of the PHQ-9 scores according to clinical parameters of infertility.

Variables	n (%)	PHQ-9 Median (min-max)	p
Cause of infertility			0.791 [†]
Diminished ovarian reserve (DOR)	25 (4.7)	2.0 (0-8)	
Male factor	88 (16.5)	3.0 (0-27)	
Male-female factor	12 (2.3)	5.0 (0-8)	
Ovulatory dysfunction	147 (27.6)	4.0 (0-21)	
Endometriosis	74 (13.9)	3.5 (0-16)	
Unexplained	187 (35.1)	4.0 (0-24)	
Duration of infertility			0.608 [*]
≥ 5 years	271 (50.8)	4 (0-24)	
< 5 years	262 (49.2)	4 (0-27)	
Kind of programs			0.103 [†]
Natural conception	276 (51.8)	4.0 (0-21)	
IUI	116 (21.8)	3.5 (0-27)	
IVF	141 (26.5)	3.0 (0-24)	
Previous ART failure			0.420 [*]
Yes	308 (57.8)	4.0 (0-27)	
No	225 (42.2)	4.0 (0-21)	
Delayed treatment due to COVID-19			0.032 [†]
No	302 (56.7)	4.0 (0-27)	
Yes	209 (39.2)	4.0 (0-21)	
Willingness to continue the treatment			0.474 [†]
No	26 (4.9)	5.0 (0-12)	
Yes	505 (94.7)	4.0 (0-27)	
Maybe	2 (0.4)	8.5 (3-14)	

^{*}Mann-Whitney U test

[†]Kruskal-Wallis test

Anxiety and fear related to the COVID-19 pandemic

This study revealed a complete overview of the anxiety and fear associated with the COVID-19 pandemic in infertility patients (Table 3). Less than a quarter (14.1%) of patients had COVID-19 infection history, with 9.8% having no symptoms. Most patients experienced concerns about the suspension of fertility treatment due to COVID-19 infection (34.1%). Nevertheless, 2.6% of patients were not afraid of contracting COVID-19. Patients with a history of asymptomatic COVID-19 infection were found to have a significantly higher median PHQ-9 score (7.0 (0-18)) (p<0.05).

The response distributions of the FCV-19 questionnaires (FCV-1 and 2)

We analyzed the patient's perception of COVID-19. FCV-1 was composed of general questions related to fear and anxiety of COVID-19 infections. While

FCV-2 contained specific questions regarding infertility and future pregnancy during the pandemic. We demonstrated that around 90.3% of the patients were worried about the COVID-19 pandemic and 81.6% experienced uncomfortable thinking about COVID-19. Almost all patients took special precautions to avoid contracting COVID-19 infection (97.0%) and were afraid their family and friends were infected with COVID-19 (91.2%). However, more than half of the participants (54.8%) agreed that the health authorities in Indonesia had not made the maximum effort to deal with COVID-19 (Table 4).

Based on the distribution of patients who responded to the FCV-2 questionnaire, anxiety about the possibility of not being able to conceive was an important consideration affecting 70.7% of patients. Most respondents were worried about contracting COVID-19 during pregnancy (87.2%), infertility treatment having to be

postponed due to infection (80.5%), and their baby being infected with COVID-19 (68.1%). On the other hand, 76% of respondents were concerned that delaying treatment would reduce their chances of getting pregnant, with 51.8% of them worried about the clinic closure during the pandemic. We demonstrated that 19.0% of patients lost hope of conceiving due to the pandemic. However, most patients (74.7%) acknowledged that the healthcare providers had provided informative details regarding the risk of COVID-19 infection during pregnancy. Approximately 27.1% favored freezing the embryo and 37.9% reported financial difficulties during the pandemic. Likewise, 33.0% experienced treatment postponement due to financial problems (Table 5). We further analyzed the association between FCV-1 and 2 with PHQ-9 scores. The median total score of FCV-1 and 2 was 50 (23-70) and 48 (21-70), respectively. There was a statistically significant correlation between FCV-1, FCV-2 and PHQ-9 scores (p<0.001) (Table 6).

Analysis of multivariate regression of the study subjects toward COVID-19 infections

Multiple regression with backward elimination and logistic regression method were performed to determine the variables that could predict depression status in patients. Low income, delayed treatment due to COVID-19, and FCV-1 score significantly predicted the depression status in patients (p<0.001). Education, occupation, COVID-19 infection status, total FCV-2 score, and failure of infertility treatment did not significantly predict the depression status (p>0.05). The incidence of depression was 1.5 times significantly greater (OR: 1.5, 95% CI: 1.013-2.265) in patients with income ≤357 USD and age was a protective factor against depressive status in women with infertility (OR: 0.957, 95% (CI: 0.917-0.998) (Table 7).

DISCUSSION

Our study aimed to identify whether several factors related to sociodemographic characteristics, fertility status, and fear of COVID-19 were associated with depression status in women coping with infertility. A significant positive

Table 3. Anxiety and fear related to the COVID-19 pandemic.

Variables	n (%)	PHQ-9 Median (range)	p
Which one is more worrying about COVID-19?			
No fear	14 (2.6)	2.0 (0-10)	0.262 [†]
Fear of fertility treatment suspension due to COVID-19 infection	182 (34.1)	4.0 (0-27)	
Fear of COVID-19 vertical transmission	77 (14.4)	3.0 (0-21)	
Fear of COVID-19 infection	128 (24.0)	4.0 (0-21)	
Fear of inability to conceive due to delaying the treatment	132 (24.8)	5.0 (0-17)	
Hear about COVID-19			
No	11 (2.1)	5.0 (1-10)	0.614 [†]
Yes	522 (97.9)	4.0 (0-27)	
Participated in COVID-19 Seminar			
No	288 (54.0)	4.0 (0-24)	0.215 [†]
Yes	245 (46.0)	4.0 (0-27)	
Willingness of vaccination			
No	31 (5.8)	5.0 (0-12)	0.122 [†]
Yes	368 (69.0)	4.0 (0-27)	
Maybe	134 (25.1)	4.0 (0-21)	
COVID-19 infection history			
No	458 (85.9)	4.0 (0-27)	0.027 [†]
Yes	75 (14.1)	4.0 (0-18)	
With symptoms	52 (9.8)	3.5 (0-16)	
Without symptoms	23 (4.3)	7.0 (0-18)	

[†]Mann-Whitney U test

[†]Kruskal-Wallis test

Table 4. The response distributions of the FCV-19 questionnaires (FCV-1).

Statements	Strongly Disagree n (%)	Disagree n (%)	Neither agree nor disagree n (%)	Agree n (%)	Strongly agree n (%)
I am most worried about COVID-19 pandemic	5 (0.9)	19 (3.6)	28 (5.3)	276 (51.8)	205 (38.5)
It makes me uncomfortable to think about COVID-19	11 (2.1)	47 (8.8)	40 (7.5)	323 (60.6)	112 (21.0)
My hands become clammy when I think about COVID-19	138 (25.9)	234 (43.9)	112 (21.0)	40 (7.5)	9 (1.7)
I am afraid of losing my life because of COVID-19	30 (5.6)	111 (20.8)	117 (22.0)	177 (33.2)	98 (18.4)
I become nervous or anxious when watching news and stories about COVID-19 on social media	37 (6.9)	118 (22.1)	102 (19.1)	216 (40.5)	60 (11.3)
I cannot sleep because I am worried about getting COVID-19	149 (28.0)	199 (37.3)	116 (21.8)	55 (10.3)	14 (2.6)
My heart races or palpitates when I think about getting COVID-19	139 (26.1)	186 (34.9)	123 (23.1)	72 (13.5)	13 (2.4)
I take precautions to avoid contracting COVID-19 infection, namely washing my hands, keeping my distance, avoiding touching objects in public places such as doorknobs	2 (0.4)	4 (0.8)	10 (1.9)	111 (20.8)	406 (76.2)
I keep up with COVID-19 news constantly	5 (0.9)	46 (8.6)	125 (23.5)	246 (46.2)	111 (20.8)
I have once prepared savings for daily needs because of COVID-19 pandemic.	28 (5.3)	66 (12.4)	77 (14.4)	244 (45.8)	118 (22.1)
In my opinion, COVID-19 is more dangerous than other seasonal flu	8 (1.5)	13 (2.4)	54 (10.1)	272 (51.0)	186 (34.9)
In my opinion, health authorities have not made maximum effort to deal with COVID-19	29 (5.4)	99 (18.6)	113 (21.2)	180 (33.8)	112 (21.0)
I am afraid COVID-19 infected my family and friends.	2 (0.4)	6 (1.1)	39 (7.3)	275 (51.6)	211 (39.6)
I do extra precautions compared to others to prevent COVID-19 transmission	5 (0.9)	17 (3.2)	77 (14.4)	290 (54.4)	144 (27.0)

Table 5. The distributions of the answer of the questionnaires related to fertility treatment during pandemic of COVID-19 (FCV-2).

Statements	Strongly Disagree n (%)	Disagree n (%)	Neither agree nor disagree n (%)	Agree n (%)	Strongly agree n (%)
I am afraid of getting infected by COVID-19 during pregnancy	6 (1.1)	21 (3.9)	41 (7.7)	264 (49.5)	201 (37.7)
I am afraid of not being able to conceive	40 (7.5)	53 (9.9)	63 (11.8)	167 (31.3)	210 (39.4)
I am afraid my infertility treatment being postponed because COVID-19 suddenly infected me	16 (3.0)	38 (71.1)	50 (9.4)	229 (43.0)	200 (37.5)
I am afraid that postponing my infertility treatment during the COVID-19 pandemic will decrease my chance to get pregnant.	21 (3.9)	46 (8.6)	61 (11.4)	213 (40.0)	192 (36.0)
I am afraid if I am pregnant, my baby will get infected by COVID-19	20 (3.8)	54 (10.1)	96 (18.0)	215 (40.3)	148 (27.8)
Temporary closing of IVF clinic during pandemic makes me lose my hope to have children	40 (7.5)	82 (15.4)	135 (25.3)	165 (31.0)	111 (20.8)
I almost give up on having children because of COVID-19	176 (33.0)	133 (25.1)	123 (23.1)	74 (13.9)	27 (5.1)
I am afraid hospitals do not have suitable protocols to prevent the infection	60 (11.3)	123 (23.1)	108 (20.3)	166 (31.1)	76 (14.3)
I prefer consultation via telehealth or telemedicine than directly meeting the doctor	66 (12.4)	162 (30.4)	176 (33.0)	91 (17.1)	38 (7.1)
Doctors or health care providers have given informative details on COVID-19 risk to pregnancy	9 (1.7)	38 (7.1)	88 (16.5)	291 (54.6)	107 (20.1)
I'd rather choose egg or embryo freezing during pandemic	65 (12.2)	124 (23.3)	200 (37.5)	100 (18.8)	44 (8.3)
I face financial problem during COVID-19 pandemic	33 (6.2)	134 (25.1)	164 (30.8)	127 (23.8)	75 (14.1)
I postpone my infertility treatment because of financial problems during the pandemic	58 (10.9)	148 (27.8)	151 (28.3)	119 (22.3)	57 (10.7)

Table 6. Correlation between FCV-1 and 2 and the PHQ-9 scores.

Variables	Total score of FCV-1	Total score of FCV-2
PHQ-9 (median (range))	50 (23-70)	48 (21-70)
4 (0-27)		
<i>p</i> -value	0.001 [‡]	<0.001 [‡]

[‡]Spearman correlation test

correlation was found between FCV-1 and FCV-2 scores and PHQ-9 scores. Low income, delayed treatment, and FCV-1 score were significant determinants of depression level in patients with infertility. We demonstrated that the patients' age significantly impacted the PHQ-9 score, with a higher score observed in the less than 35-year-old group. Lower stress reactions in older women may be related to a better coping mechanism.¹² Furthermore, the levels of anxiety and depression were higher in couples with previous ART failure. Feelings of anxiety and depression can be caused by women's views that the process of pregnancy and childbirth is their responsibility.¹³

A history of asymptomatic COVID-19 infection had a higher depressive status. It was reported that people infected with COVID-19 had a higher level of

depression, anxiety, and post-traumatic stress symptoms than people who were not infected. Women with COVID-19 have a higher "Perceived Helplessness" score than men with COVID-19 and controls.¹⁴ Feeling unprepared, uncertain, and having a sense of helplessness are fundamental causes of stress in COVID-19 patients.¹⁴ In addition to the distress led by the infertility issue, COVID-19 infection may worsen depression in infertility patients seeking treatment.

COVID-19 also has a considerable impact on the economic sector.¹⁵ Nearly half of workers in the manufacturing and education sectors experienced a decline in income due to pay cuts or reduced working hours. Some of them experienced unpaid leave or layoffs. Inevitably, most of the private sector workers in Indonesia underwent financial constraints during

the pandemic.⁵ This condition may lead to anxiety and depression, specifically during the pandemic.¹⁵ Women who have infertility problems are already prone to depression.¹⁶ The burden of infertility is higher in women than men due to perceived stigma in society and fear of the procedures required during infertility treatment.⁶

Depression and anxiety have long been known to be associated with infertility. These psychological problems are common in female partners.¹⁷ The COVID-19 pandemic has led to the issuance of a delayed fertility workup policy at the early stage of the pandemic.¹⁸ A study found that depressive symptoms were present in more than half of women who had delayed fertility therapy due to the COVID-19 pandemic. This suspension causes a substantial reduction in the quality of mental health.¹⁹ As women age, the ovarian reserve declines, resulting in decreased chances of getting pregnant.²⁰ Women delaying fertility therapy had a higher FCV-19 score than those who decided to resume the treatment. It has been proven that suspension of fertility

Table 7. Multivariable logistic regression analysis for predictors of depression status based on PHQ-9.

Independent variables	PHQ-9			
	B	Standardized Beta	OR (95% CI)	p
Age	-0.072	-0.082	0.957 (0.917-0.998)	0.062
Income (≤357 USD versus others)	1.171	0.126	1.515 (1.013-2.265)	0.004
Delayed treatment due to COVID-19	0.732	0.085	1.238 (0.851-1.801)	0.047
FCV-1 score	0.061	0.107	1.006 (0.976-1.037)	0.012

workup may result in disappointment and concerns of decreased possibilities of conceiving, exceptionally in older women. However, most women with infertility decided to continue fertility treatment despite the pandemic,^{10,21} as shown in this study.

Fear of COVID-19, low income, and delayed treatment were also predictors of depressive symptoms in infertility patients. Women experience anxiety regarding the decision to get pregnant during the pandemic due to concerns about adverse effects on the fetus,²² the possibility of COVID-19 infection, and financial constraints.²¹ A higher likelihood of fear of COVID-19 was evident among women, married people, and those with a lower level of education.²³ Nonetheless, the existence of the internet to disseminate information regarding COVID-19 can positively affect lowering FCV-19 scores and the risk of depression and anxiety in pregnant women.²⁴

Studies investigating the psychology of women with infertility during the pandemic have been carried out in various countries. Higher anxiety is shown in women over 35 years old. A higher value of FCV-19S was observed in women who postponed infertility treatment during the pandemic, based on research in Turkey using the Spielberger State-Trait Anxiety Inventory (STAI-T and STAI-S) and FCV-19S questionnaires.¹⁰ Another study conducted in Italy using the Generalized Anxiety Disorder-7 (GAD-7) and PHQ-9 questionnaires had similar findings. Levels of anxiety and depression were higher in women who experienced treatment delays, especially those over 35 who had previously attempted IVF.¹⁷ Infertility treatment delays were linked to the high median level of depression symptoms in Canada and the United States as analyzed using PHQ-9 and other questionnaires related to anxiety, pessimism or optimism, helplessness or acceptance, and infertility-

specific coping responses.¹⁹

This study certainly has its strengths, given the large sample size. However, its cross-sectional design can limit the evaluation of causality between patient characteristics and other independent variables. The investigation was limited to assessing the relationship between fear of COVID-19 and depression in women with infertility and predicting the factors affecting the depression. It must be considered that research findings can be impacted by the fact that several variables may influence depressive disorders; the symptoms can manifest even before the pandemic, and assessments carried out during the restriction on community activities began to loosen up. Similar notes were also emphasized in another research on the psychological effects on women undergoing delayed infertility therapy during COVID-19 pandemic, in which a causal relationship would be difficult to assess given that depressive symptoms may have occurred before the study or even the pandemic.²⁵ The design could also result in insufficient patient characteristics information before the pandemic. Using an online questionnaire might restrict the sample to subjects who have access to computers, mobile devices, and the internet rather than the general population. Further research is still needed to assess changes in depression state before and during the pandemic and whether fear of COVID-19 can cause depression in women with infertility.

CONCLUSION

In conclusion, although perception and knowledge of COVID-19 infection may be associated with the levels of depression in infertility patients, the enthusiasm to continue treatment is not disturbed. Factors attributed to emotional stress are primary infertility, older age, and duration of infertility. The existence of

COVID-19 pandemic has given rise to new, unexpected stressors that may aggravate their psychological condition. Accordingly, monitoring the mental health status of couples experiencing infertility is indispensable to improving the success rate of infertility treatment. However, the length and implications of the pandemic are unpredictable; thus, the outcomes of this study may not reflect the sustained consequences of the COVID-19 pandemic on the psychological well-being of women with infertility.

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CONFLICT OF INTEREST

The author reports no conflicts of interest in this work.

ETHICAL CONSIDERATION

This study was approved by the Faculty of Medicine, Universitas Indonesia Ethics Committee with the reference number: KET-1464/UN2.F1/ETIK/PPM.00.02/2020.

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AUTHOR'S CONTRIBUTION

M.M. was responsible for the conception, study design, data acquisition and analysis, drafted, wrote, revised, and critically reviewed the manuscript. E.B. contributed to data analysis, drafted, revised, and critically reviewed the manuscript. A.S. contributed to data acquisition and analysis and drafted the manuscript. P.D.G. contributed to data acquisition and analysis and drafted the manuscript. V.S. contributed to study design. A.K.H. contributed to study design.

K.S. contributed to critically review and revise the manuscript. G.P. contributed to critically review and revise the manuscript. R.M. contributed to critically review and revise the manuscript and supervisory support. A.H. contributed to conception of this study and supervisory support. B.W. led the supervisory support and contributed to conception of this study. All authors read and approved the final manuscript.

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