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## Authors' Affiliation:

<sup>1</sup>Senior Registrar, Obstetrics and Gynecology, King Abdulah Medical Complex, Jeddah, Saudi Arabia

Email: Dr.rawanalhazmi@gmail.com

<sup>2</sup>Senior Registrar, Obstetrics and Gynecology, King Saud University Medical City, King Saud University, Riyadh, Saudi Arabia

Email: mbokhari1990@gmail.com

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# Perception of poor prognosis and psychological impact on the infertile couples who stop IVF therapy: Cross sectional scientific perspective

Rawan Ahmad Alhazmi<sup>1</sup>, Mahdya Bukhari<sup>2</sup>

## ABSTRACT

The goal of this study is to examine the mental health of infertile men and women who's in-vitro-fertilization-(IVF) treatment halted or delayed due to the perception of poor prognosis. *Materials and methods:* Couples whose IVF procedures stopped or delayed because of the perception of poor prognosis sent an internet survey between June and August 2022. The Generalized-Anxiety-Disorder-7 (GAD-7) and Patient-Health Questionnaire-9 were used to measure the presence and severity of symptoms indicative of anxiety and/or depression (PHQ-9). Subjects with prior psychiatric illnesses were not allowed to participate. Informed consent and IRB approval (# 9690/3/KB11). *Results:* In all, 524 of the 646 patients who took the survey did so. Women were considerably more likely to experience anxiety and/or depressive symptoms, especially if they were older than 35 and had previously tried IVF. The incidence of these psychological symptoms was substantially correlated with the amount of time spent each day reading news about perception of poor prognosis, with evidence of a psychiatric condition and in females, with a diagnosis of endometriosis, uterine fibroids or low ovarian reserve. *Conclusions:* The perception of poor prognosis has had a profound psychological impact on the infertile couples who should have received IVF therapy. IVF clinics must to routinely provide these couples with sufficient psychological therapy to enhance mental wellness.

**Keywords:** Perception, Poor Prognosis, Psychological Impact, Infertile Couples, IVF Therapy

## 1. INTRODUCTION

Practitioner suggestions in reproductive medicine included delaying non-urgent diagnostic tests, elective surgical procedures and the commencement of assisted reproductive technology (ART) therapies (Volgsten et al., 2008). The American-Society-for-Reproductive-Medicine-(ASRM) and the European-Society-of-Human-Reproduction-and-Embryology-(ESHRE)

specifically recommended stopping new fertility procedures, such as ovulation induction, intrauterine insemination (IUI) and in-vitro-fertilization-(IVF), as well as non-urgent gamete cryopreservation and canceling all fresh or frozen embryo transfers in the early stages. Patients who were "in-cycle" at the time or needed urgent fertility preservation because of cancer treatment were the exceptions (La-Rosa et al., 2020).

Societies in Europe have lately permitted the gradual reintroduction of ART operations thanks to effective mitigation efforts (Peterson et al., 2014). Stress from infertility is already present. It is well known that the experience of infertility has a profound effect on both spouses' psychological health. In fact, infertile couples typically encounter concerns including poor self-esteem, sexual discomfort, sadness, guilt, anxiety and relationship problems. Additionally, the failure of ART methods might worsen a person's or a couple's mental health (Stern et al., 2022). Perception of poor prognosis has significantly affected everyone's daily lives due to quarantine, social isolation, travel restrictions, treatment cancellation and constant fear for their own and their families in danger (Stern et al., 2015).

Couples who should have had IVF treatment are likely to have experienced emotional effects as a result of this sense of worry, anxiety and despair. Infertile individuals whose IVF procedures were stopped or delayed because of the perception of poor prognosis were the subject of this cross-sectional study, which sought to examine their psychological state (Carson and Kallen, 2021). We specifically expected that because women are more vulnerable to the psychological effects of infertility and its therapies than males, the perception of poor prognosis experience had a substantial positive impact on these couples' emotions of worry and melancholy.

## 2. MATERIALS AND METHODS

All couples who were sent to our facility and whose IVF procedures had been halted or delayed because of the perception of poor prognosis were included in this cross-sectional analysis. Between 10 June and 1 August 2022, patients were identified and demographic information was prospectively gathered using specialized software. The study protocol (415/2022) was authorized by the regional Ethical Committee and all research was carried out in accordance with the necessary policies and laws. Informed consent and IRB approval (# 9690/3/KB11)

All of the ladies provided their informed permission for the study's data collection and usage. Infertile couples who were sent to our facility received an email with a link to an anonymous online survey on the Google Forms web application. Until the completion of the research period, a reminder email was sent out every week. After a brief introduction, all participants were informed of the survey's goal. At the start, participants were required to sign a consent form for the privacy policy. There were no incentives given and survey participation was entirely voluntary. When a pair only provided a single response, we nonetheless included that response in the study.

The survey was divided into two parts: The first part used the Generalized-Anxiety-Disorder-7 (GAD-7) and the Patient Health Questionnaire-9 (PHQ-9) to measure the presence and severity of symptoms suggestive of anxiety and depression and the second part assessed patients' opinions on restarting IVF treatment or even switching referral ART centers. The investigation did not include those who had previously received a DSM-V diagnosis for a mental condition (Youseflu et al., 2020).

The GAD-7 is a validated questionnaire with seven items that measure anxiety symptoms according to DSM-IV criteria. Cutoff values for mild or moderate or severe anxiety symptoms are 5, 10 and 15, respectively, on the entire scale, which has a range of 0 to 21 (Jordan et al., 2017). The PHQ-9 is a validated measure for evaluating depressive symptoms that is based on nine items that link to DSM-IV criteria. Cutoff scores for mild, moderate, moderately severe and severe depressive symptoms are 5, 10, 15 and 20, respectively, on the total scale, which has a range of 0 to 27 (Maroufizadeh et al., 2019). "Not at all", "a few days", "more than half the days" and "almost every day" are the available responses for both surveys and they are graded as zero, one, two and three, respectively.

Results were downloaded in the form of an Excel-categorized CSV file after the deadline for questionnaire submissions (version 16.39; Microsoft Corporation, Redmond, USA). Utilizing Statistics Package for Social Sciences, statistical analysis was performed (SPSS, version 24.0 Chicago, IL, USA). The CHERRIES Guidelines (Eysenbach, 2004) were followed for reporting the survey's findings.

### Data analysis

The Kolmogorov-Smirnov test was used to confirm the normality of continuous data. Descriptive statistics were presented as the mean, standard deviation or median and interquartile range depending on the distribution of the variables (IRQ). For the analysis of continuous data, the paired or unpaired t-test was used and the chi-squared test for categorical data. The differences in

dependent variables between two independent groups—which were not normally distributed—were compared using the Mann-Whitney U test. The odds ratio (OR) with a 95% confidence interval (CI) of (categorical or continuous) independent factors and one dichotomous dependent variable was examined using logistic regression technique. The Spearman's Rho test was used to assess correlation measurement results. Statistical significance was defined as a two-sided p-value of 0.05.

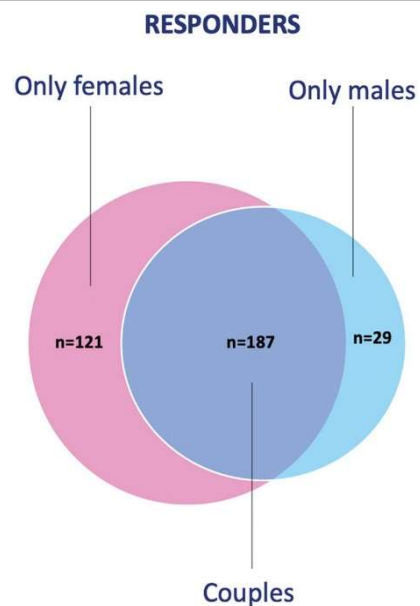
### 3. RESULTS

Out of 646 patients, 524 (308 women and 216 males) finished the survey (response rate: 81.1%; 95% CI, 77.7-84.1%; Figure 1). The men and women who participated in the study had mean (SD) ages of 37.3 (4.6) and 38.4 (6.2), respectively. 187 had a median of two prior unsuccessful IVF cycles (range, 0–8); 56 couples (29%), heterologous fertilization was being used. Table 1 lists the additional demographic details of the research population. Anxiety, depression or both were common in 45.5% of women (140 of 308; 95% CI, 39.8-51.2%) and men (67 of 216; 95% CI, 24.9-37.7%) respectively.

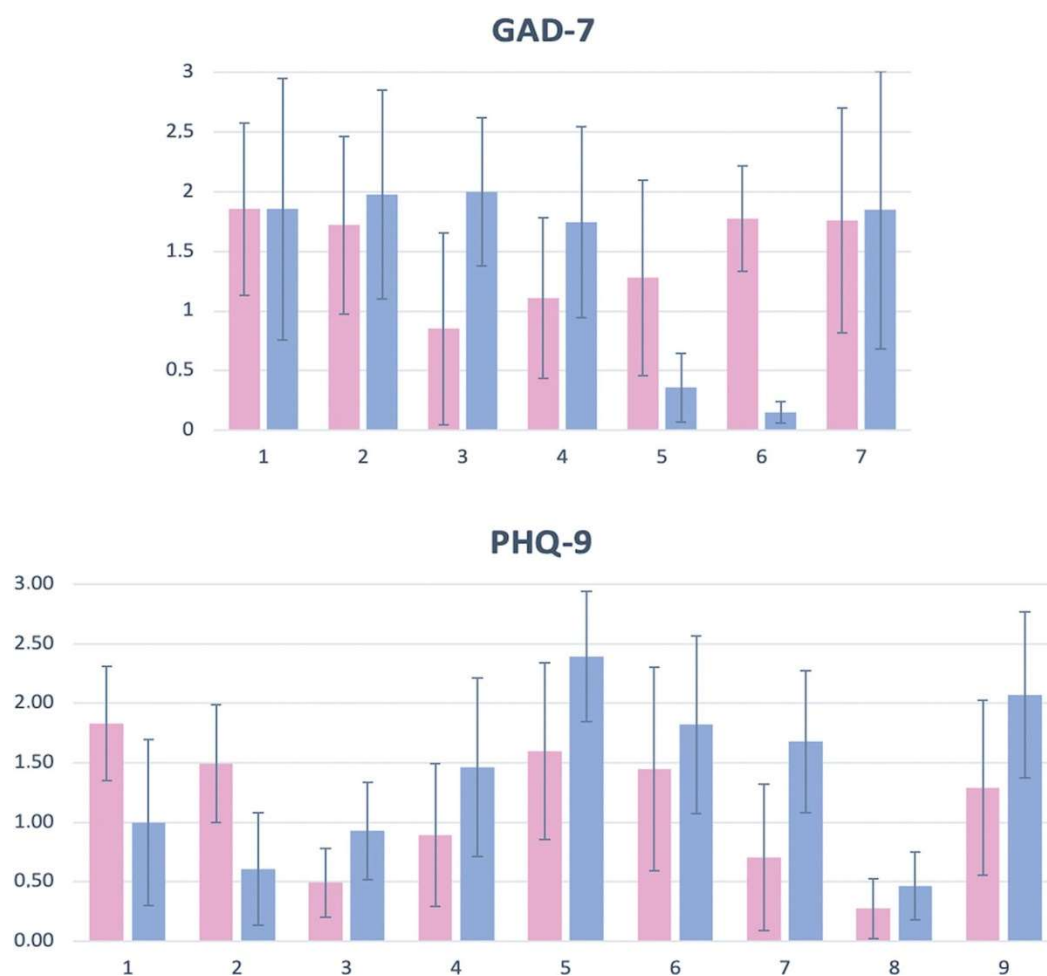
**Table 1** Demographic characteristics of the study population

Characteristics	Females (n1/4 308)	Males (n1/4,216)
Age, mean ( $\pm$ SD)	37.3 ( $\pm$ 4.6)	38.4 ( $\pm$ 6.2)
BMI, mean ( $\pm$ SD)	24.5 ( $\pm$ 3.1)	24.2 ( $\pm$ 3.3)
Smoking, n (%)	56 (18.2)	37 (17.2)
Ethnicity, n (%)		
<i>White</i>	279 (90.6)	198 (91.7)
<i>Asian</i>	9 (2.9)	4 (1.9)
<i>Hispanic</i>	13 (4.2)	8 (3.7)
<i>Black</i>	7 (2.3)	6 (2.8)
Previous children, median(range)	0 (0-3)	0 (0-2)
Highest education n (%)		
<i>Post-secondary and tertiary</i>	124 (40.3)	81 (37.5)
<i>Upper secondary</i>	146 (47.4)	112 (51.9)
<i>Lower secondary or less</i>	38 (12.3)	23 (10.6)
Couples (n1/4 187)		
Heterogonous fertilization n (%)	56 (29.9%)	
Previous failed IVC cycle, median (range)	2 (0-8)	
Duration of infertility, mean (%)	3.6 ( $\pm$ 2.1)	
Etiology of infertility, n (%)		
<i>Female factor</i>	81 (43.3)	
<i>Male factor</i>	62 (33.2)	
<i>Mixed</i>	26 (13.9)	
<i>Unexplained</i>	26 (13.9)	

This frequency was substantially greater in women than in males ( $p$  0.001), in women over the age of 35 (49.3% vs. 46.3%,  $p$  0.036) and in women who had previously tried IVF (57.7% vs. 24.1%,  $p$  0.001). A median total score of 11 on the GAD-7 (interquartile range, IQR: 8–15) indicated anxiety in 75 women (24.4%; 95% confidence interval, 19.7–29.5%) and a median total score of 9 in 39 males (18.1%; 13.2-22.9%) (Interquartile range, IQR: 7–13; Figure 2). The majority of the time, anxiety was mild in males ( $n$  32; 82.1%; 95% CI, 66.5-92.5%; Table 2) and moderate in women ( $n$  46; 61.3%; 95% CI, 49.4-72.4%).



**Figure 1** Venn illustration showing the responders to the investigation



**Figure 2** Mean values of answers to specific items at GAD-7 and QHP-9 questionnaires

With a median total score of 4 (IQR: 3-13) on the PHQ-9, depression was found in 65 women (21.1%; 95% CI, 16.7-26.1%) and in 28 males (13.0%; 9.8-18.2%) with a median total score of 3 on the PHQ-9 (IQR: 3-9). Males were more likely to have moderately

severe depression than women were (n 3 vs. n 0; 60.1% vs 0%; p 0.007; Table 2), however both genders had moderate intensity depression in the majority of cases (n 46; 70.1%; 95% CI, 58.2-81.4%) and men (n 17; 60.1%; 40.6-78.5%).

**Table 2** Symptom severity of anxiety and depression in the study population

	Females			Males				Patients		
Symptom Severity	Number	Absolute %	Cumulative %	Number	Absolute %	Cumulative %	p <sup>ω</sup>	Number	Absolute %	Cumulative %
ANXIETY (GAD-7)										
Mild	26	8.4	8.4	32	14.9	14.9	<0.001	58	11.1	11.1
Moderate	46	14.9	23.3	7	3.2	18.1	<0.001	53	10.1	21.2
Severe	3	1.1	24.4	0	0	18.1	0.206	3	0.6	21.8
TOT	75	24.4	–	39	18.1	–	–	114	21.8	–
DEPRESSION (PHQ-9)										
Mild	19	6.2	6.2	7	3.2	3.2	0.707	26	5	5
Moderate	46	14.9	21.1	17	7.9	11.1	0.397	63	12	17
Moderately severe	0	0	21.1	3	1.4	12.5	0.007	3	0.6	17.6
Severe	0	0	21.1	1	0.5	13	0.123	1	0.1	17.8
TOT	65	21.1	–	28	13	–	–	93	17.8	–

GAD-7: Generalized Anxiety Disorder-7; PHQ-9: Patient Health Questionnaire-9. <sup>ω</sup> Comparison of symptom severity between males and females

Men exhibited a very weak positive association between these scores (R 0.110; p 0.001), whereas women had a somewhat positive correlation between GAD-7 and PHQ-9 scores (R 0.339; p 0.05). Additionally, 13 males (6.0%; 95% CI, 3.2-10.1%) and 25 women (8.1%; 5.3-11.8%) reported having concurrent feelings of anxiety and despair. The prevalence of anxiety and/or depression was greater in women with a female component of infertility than in women without a female element of infertility (46.7% vs. 21.8%, p 0.001) and it was also higher in males with and without a male factor of infertility (29.2% vs. 16.5%, p 0.036).

When anxiety and/or sadness were present, they were substantially correlated with the amount of time spent each day reading news about the perception of poor prognosis (> 1 h, p 0.034) and paired with signs of psychiatric disorder (p 0.017; Table 3). Anxiety and/or sadness were not significantly correlated with education level or prior parity (p 0.383 and p 0.679, respectively). In females, endometriosis diagnosis (p 0.001), uterine fibroids diagnosis (p 0.040) and low ovarian reserve (p 0.032) were all substantially linked with the prevalence of symptoms indicative of anxiety and/or depression. Both a previous unsuccessful IVF cycle and the number of prior unsuccessful IVF cycles did not directly correlate with the prevalence of these psychological symptoms (p 0.910) or R 0.049; p 0.388, respectively. Overall, 75 men (36.6%; 95% CI, 30.1-43.4%) and 121 women (39.3%; 33.8-45.0%) stated that they still wanted to have IVF therapy despite the perception of poor prognosis. If they knew when they could restart their IVF treatment, 239 women (77.6%, 95% CI, 72.5-82.1%) and 162 men (70.1%, 95% CI, 63.8-76.1%) said they would feel more at ease; 118 women (38.2%, 95% CI, 32.9-44.0%) and 88 men (40.7%, 95% CI, 34.1-47.6%) said they would switch IVF clinics if they could restart their IVF treatment

**Table 3** Signs of psychiatric disorder

Variable	B	SE	Wald	Odds ratio	95% CI	p
Females/males						
Period spent on COVID-19 related update per day (>1 hour per day)	0.548	0.259	4.496	1.73	1.042–2.017	0.034
Partner with evidence of psychological disorder	0.699	0.293	5.709	2.012	1.134–3.569	0.017
Females						
Age	0.523	0.259	4.09	1.687	1.016–2.801	0.043
Poor ovarian reserve	0.508	0.261	3.789	1.661	0.997–2.770	0.052
Diagnosis of endometriosis	0.598	0.287	4.351	1.819	1.037–3.192	0.037
Diagnosis of uterine fibroids	1.116	0.293	14.478	3.051	1.718–5.421	<0.001

#### 4. DISCUSSION

In order to reallocate personnel and resources to address the perception of poor prognosis, a drastic overhaul of healthcare delivery has included a halt to IVF rounds. To the best of our knowledge, this is the first research examining the mental health of infertile people whose IVF procedures have been suspended or delayed as a result of the perception of poor prognosis (Wely et al., 2006). This study found that among infertile females experiencing IVF, the perception of poor prognosis was associated with a not insignificant increase in the detection of anxiety and depressive symptoms. More over one-third of the patients sent to our IVF facility experienced signs of anxiety or depression, according to our data. In addition, more patients (men: 18.1% vs. 13.0%; women: 24.4% vs. 21.1%) reported anxiety than depression (Stern et al., 2022).

In contrast, depression had a moderate intensity in both sexes (women: 70.1%; men: 60.1%), with anxiety being more frequently moderate in women (61.3%) and mild in males (82.1%). But just 1% of men and women with signs of these psychiatric problems displayed severe symptoms (Table 2). These findings are consistent with the body of research, which indicates that depression and anxiety are commonly linked to infertility and may get worse during ART (Prasad et al., 2020). It's interesting to note that stress and anxiety connected to fertility have been observed to be positively correlated with low feeling of personal control and avoidant coping style (La-Rosa et al., 2020). Instead, ratings for depressed symptomatology and stress linked to fertility may be adversely correlated with a problem-appraisal coping style.

The majority of infertile women in the general population probably struggle with sadness and anxiety, but they seldom seek help (Facchin et al., 2015). Major depression was the most prevalent mood disorder in 23,557 women undergoing their first IVF cycle and it was present in 10.9% of females and 5.1% of males, according to cohort study (Rooney and Domar, 2018). Any anxiety disorder was present in 14.8% of females and 4.9% of males. Another study that included 1090 women and men who had been referred to a fertility clinic found that major depressive disorder was present in 8.5% of females and 2.2% of males, while anxiety was present in 14.8% and 8.9% of cases. Approximately 35% of both women and men had at least two psychiatric disorders diagnosed concurrently (Vitale et al., 2017). Another observational trial of 226 patients seeking therapy for infertility in five reproductive clinics revealed increased incidence of depression 66% and anxiety 76%; these psychological disorders were more prevalent in women who did not have a successful ART operation (Fauser et al., 2019).

An unprecedented worldwide event, the perception of poor prognosis is fundamentally altering everyone's outlook and way of life. The perception of poor prognosis is causing enormous stress in contemporary history (Youseflu et al., 2020). It was an unforeseen incident and the effects are still posing a threat to everyone's present and future, including the possibility of losing daily life owing to the lockdown, monetary instability and social isolation. In this context, recent researches have proven the significant psychological effects of the emergency caused by the perception of poor prognosis in various segments of the community, including students and healthcare workers (Jordan et al., 2017).

In this case, it is conceivable that the perception of poor prognosis-related sensations of worry, anxiety and despair may have had a substantial effect on the emotional health of couples who ought to have had IVF therapy during the emergency. In this context, statistics from an online survey distributed to 10,481 patients who attended a sizable university affiliated infertility practice given in a brief communication released (Maroufzadeh et al., 2019).

Respondents identified infertility as the most common top stressor, generating anxiety and despair, at three separate time points. Perception of poor prognosis caused stress at a rate that was comparable to infertility (sixty three percent and sixty six percent, respectively). Only 6% of patients in this survey agreed that IVF should not be used to treat infertility. In line with these findings, our study revealed a strong relationship between the frequency of anxiety and/or sadness and the daily amount of time spent reading about perception of poor prognosis (Eysenbach, 2004).

Recent research has looked into how perception of poor prognosis affected people who were referred to IVF clinics. The perception of poor prognosis had a moderate-to-severe psychological effect on patients who were infertile. Women were more emotionally upset, anxious and sad than males, Gourounti et al., (2012) which is consistent with our results. 101 women whose ART cycles were delayed due to perception of poor prognosis responded to a second Turkish online poll, which revealed that women over 35 had considerably higher state-anxiety levels. The existence of clinical state-anxiety was strongly predicted, as it was in our trial, by decreased ovarian reserve and a prior ART failure (Herbert et al., 2010).

In 92 women from Canada and the United States, new research looked at the psychological effects of the perception of poor prognosis stoppage of reproductive treatments. Additionally, the study looked at psychosocial indicators of improved or poor mental health. More than 50% of participants agreed that clinically significant depression symptoms existed. The authors demonstrated that a higher psychosomatic condition during this time was positively connected with a number of psychosocial characteristics, including lower levels of defensive pessimism, more infertility acceptance, better quality social support and more



social support seeking (Cesta et al., 2016). 168 patients whose, reproductive treatment was stopped because to the perception of poor prognosis in a tertiary hospital were included in a cross-sectional questionnaire research. Feeling helpless after treatment suspension was linked to higher distress, while higher self-mastery and more significant perceived social support were linked to lower distress, whereas demographic factors like age-marital-status-parity-economic-status or duration of treatments did not have a significant impact (Volgsten et al., 2008).

The danger to the aim of parenting and the uncertainty around clinic closure were considered to be stressful factors. However, most patients have been able to adapt by employing thought-management techniques (such as diversion and positive thinking), being physically and psychologically prepared for the next therapies, fortifying their social networks and staying current (Pasch et al., 2016). In our survey, more than two-thirds of both men and women said that knowing the IVF treatment's resumption date would reassure them. In line with our study, several authors have shown that a significant number of patients would continue IVF therapy despite the perception of poor prognosis (Golmakani et al., 2019).

Males receiving ART therapy may face additional psychological effects due to the lock-down of andrological services. It is known that men undergoing reproductive treatment may additionally feel anxious and stressed. In reality, our study found that 30.6% of males suffered from anxiety or depression; as a result, it is important to consider the physiological and psychological effects of not providing andrological care (Karimzadeh et al., 2017).

In particular due to perception of poor prognosis, psychological therapies may have a key role in reducing psychological suffering in patients referred to IVF institutions (Peterson et al., 2012). The most effective method to accomplish both objectives may be cognitive-behavioral. To help couples enhance their quality of life and mental health even more due to perception of poor prognosis, IVF centers must step up their psychological therapy (Peterson et al., 2014). To do this, particular techniques may give support at various points along the treatment trajectory via a variety of channels (such as handouts, a website and personal referrals) and different providers (i.e., psychologists, physicians, medical assistants, nurses). Our study offers several significant advantages. It is one of the first studies to examine the psychological effects of the perception of poor prognosis on infertile individuals whose IVF procedures have been discontinued or delayed, as was already mentioned. Additionally, because of the size of our sample, we may say that our findings are significant.

There are certain restrictions, though. In order to assess the influence of the perception of poor prognosis in a mentally healthy group of patients undergoing IVF, participants with previous psychiatric illnesses identified using the DSM-V have been eliminated from the sample. However, it cannot be fully ruled out because the individuals had never before displayed symptoms of anxiety or sadness. In our facility, psychological testing and counseling are frequently provided to IVF couples and in the event that a patient is suspected of having a mental illness, they are subjected to a psychiatric evaluation using the DSM-5 criteria. However, because we did not analyze the incidence of anxiety and/or depression in patients undergoing IVF at our facility, we are unable to pinpoint a precise causal link between the analyzed variables.

Furthermore, because we employed an online questionnaire with self-reported measures, it was hard to rule out the possibility that self-report bias had an impact on our findings. Finally, despite the large number of responders, our demographic might not be a representative one overall. The poll was only given out in our neighborhood; therefore, it's possible that the results cannot be applied to all of Italy or other nations. In the next months, a longitudinal follow-up would be useful for monitoring changes in the levels of anxiety and depression at various phases.

## 5. CONCLUSION

The perception of poor prognosis has had a major psychological impact on infertile couples whose IVF procedures were delayed or stopped due to the emergency, according to the study's findings. To enhance their quality of life and mental health as well as to minimize the psychological effects of the perception of poor prognosis, it is crucial that IVF clinics consistently provide these couples with proper psychological treatment.

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### Author Contributions

Mahdya and Rawannot did all the steps of research from conceptual framework till the statistical analysis.

### Ethical approval

The study was approved by the Medical Ethics Committee of AMZE. Ethical approval code (X# 9690/3/KB11)

### Informed consent

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

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This study has not received any external funding.

### Conflict of interest

The authors declare that there is no conflict of interests.

### Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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