



## Review Article

# Quality of Life in Infertile People Forced to Suspend Assisted Reproductive Technology Treatment during the COVID-19 Global Health Emergency

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### Abstract

**Objective:** To evaluate the psycho-physical well-being of people coping with infertility who were forced to suspend ART treatment due to restrictions related to the COVID-19 global health emergency.

**Methods:** The participation to the present study was proposed to patients that were both undergoing/beginning Assisted Reproductive Technology (ART) treatment in the Centre of Reproductive Medicine, Sandro Pertini Hospital in Rome, that had to suspend their medical treatment for the COVID-19 outbreak. 30 patients gave their informed consent and filled in the following self-report measures: Coping Inventory for Stressful Situations (CISS), Dyadic Adjustment Scale (DAS), Symptom Checklist-90-Revised (SCL-90 R); Fertility Quality of Life (FertiQoL).

**Results:** Through the correlational analysis several significant associations between the quality of life and the other variables investigated emerged. Furthermore, through multiple linear regression analyses both the use coping strategies focused

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on emotion and the presence of psychopathological symptoms predicted a lower quality of life during COVID-19 pandemic.

**Conclusion:** The results support the organization of psychological interventions for people facing ART during the COVID-19 pandemic, focused on the implementation of adequate coping strategies and on the containment of psychopathological symptoms.

**Keywords:** ART; Coping strategies; COVID-19; Infertility; Quality of life

### Introduction

#### COVID-19, infertility and assisted reproductive technology

The COVID-19 pandemic is a severe global crisis that has disrupted essential aspects of life, affecting both the physical and psychological health of the people who are facing this traumatic experience [1]. Italy was the first European country to face the full force of the pandemic [2]. At the time of this paper's publication, official reports showed that 41.737 patients in Italy had died from COVID-19, with a mean age of 80 years [3].

In response to the rapid spread of COVID-19 across the country, on March 10, 2020 the Italian government imposed a national quarantine with subsequent lockdown restrictions that mandated the temporary closure of non-essential commercial activities and services. All guidelines published by reproductive medicine societies at this time endorsed cessation of infertility services with some granted exemptions for exceptional circumstances (oocyte or sperm cryopreservation or procedures in patients starting chemotherapy or radiation), with the aims of preventing both possible complications of ART treatment and possible complications from the virus on any potential pregnancy, optimizing the allocation of health care resources and promoting social distancing [4]. Therefore, couples attending an ART treatment for fertility problems had to suspend the treatment until the end of the lockdown period (May, 2020). To date, very little is known about the ways in which infertile couples who had to suspend their fertility treatment coped with this limitation and this difficult period.

A recent study investigating the impact of the COVID-19 pandemic on patients with infertility demonstrated that even in the context of the pandemic, the stress of infertility has remained significant and is a comparable stressor to the pandemic itself [5]. Given that only 6% of participants in the study agreed that infertility treatment should not be offered during the COVID-19 pandemic [5], it follows that for the other 94% of participants the suspension of treatment was experienced as a hardship. Tokgoz et al., [6] evaluated anxiety levels in women with infertility whose ART cycles were delayed due to the COVID-19 pandemic. This study showed that state-anxiety levels were significantly higher in women older than 35, those with diminished ovarian reserve, and those with longer duration of infertility. Diminished ovarian reserve and previous ART failure significantly predicted the presence of clinical levels of state-anxiety [6].

Esposito et al., [7] showed that women were more emotionally distressed, anxious and depressed than men. The COVID-19 pandemic and the recommendation to stop ART program clearly generated additional distress levels in couples coping with infertility. With that in mind, the authors of the present study concluded that the psychological impact of COVID-19 pandemic in infertile patients should not be underestimated, and a specific psychological support should be planned.

Given that social isolation (especially when it is protracted), feelings of loneliness and fear, and uncertainty about the future may increase the risk of developing psychophysical symptomatology, the COVID-19 pandemic meets criteria for a traumatic event [2]. It stands to reason that the pandemic should have presented additional burdens to people coping with infertility, as infertility itself already represents a major life crisis that threatens important life goals and that can be accompanied by a variety of psychological disorders [8]. Many people who experience infertility see it as a disruption in their developmental trajectory into adulthood as well as other personal, couple, and social domains [9-10], so their vulnerability to additional stress is likely to be significant.

### Psychological and relational features related to infertility and treatments

Studies of the negative psychological, behavioural, and social consequences of infertility have demonstrated that couples with infertility tend to experience a wide range of negative emotions, including anxiety, fear, avoidance, depression, guilt and frustration [11-14] impacting their overall life satisfaction and well-being [10,15]. The impact of fertility problems varies widely among couples including negative effects on a couple's well-being, marital relationship, and success of treatment, with some partners becoming distant from each other [10,16-20]. In other cases, the couples can benefit from facing the hardship of infertility diagnosis and treatment together [21-23]. Research has suggested that levels of agreement between partners, dyadic adjustment, and perceived intimacy and mutual support are potentially significant protective factors for psychological health among infertility patients undergoing medical treatments [9,24-26]. For example, a recent study highlighted several associations among couple characteristics, infertility-related quality of life, attachment anxiety and avoidance dimensions, with positive ART outcomes; more specifically the positive medical outcome appeared to be predicted by lower levels of avoidance within the couple relationship that is low levels of fear of dependence and interpersonal intimacy, and low need both for self-reliance and for reluctance to self-disclose within the romantic relationship [27].

Several studies have investigated the role of the various coping strategies couples use to deal with infertility, finding that strategies focused on activity and interaction with others, like problem solving, social support and positive attitude, have protective effects [28-31]. However, other studies have found that strategies focused on avoidance and passivity have a significant protective role [9,32,33]. More specifically, in conditions of both unpredictability of the outcome treatments and low control of the situation, assuming an attitude of emotional distance and passive waiting seems to play a protective role for the individual, allowing to control negative emotions. In conclusion, literature suggests that the impact of coping strategies may vary in each specific situation [34]. Many couples diagnosed with

infertility will pursue some ART treatment as a way of resolution of the blocked goal of parenting [12]. Therefore, the limitations imposed by the lockdown period may have represented a further block to the realization of the desire to become parents, possibly increasing and exacerbating the perception of loss of control, incapability to plan for the future, mood symptoms, and anxiety frequently experienced by couples with infertility [9,35].

### Aim

The aim of the present study is to evaluate the psycho-physical well-being of people with infertility who were forced to suspend their ART treatment due to the limitations imposed by COVID-19 global health emergency. Specifically, we investigated the relationships between coping strategies, dyadic adjustment, and psychophysical symptomatology with the quality of life related to fertility. We hypothesized that an avoidant coping style, including a limited use of the couple relationship as a social support source, and the presence of mood symptoms (such as depression and anxiety) would predict low quality of life.

### Materials and Methods

#### Participants

Participants were selected among the patients assisted in the reproduction Department at the Sandro Pertini Hospital in Rome.

The inclusion criteria were:

- Undergoing or beginning an ART treatment in the medical centre
- To be forced to suspend the medical treatment for the COVID-19 outbreak
- Undergoing the ART treatment for a fertility problem and not for Pre-Implantation Genetic Diagnosis (PGD)
- Understand the Italian language

Participation in the study was offered to 70 people. Among the 30 who opted to participate 76% were female and 24% were male. In terms of relationship status, 72.5 % of the participants were married and 27.5% were unmarried but living together. Ten percent of participants reported an educational level of 8 years, 38% reported 13 years and 52% reported 16 years. Seventy-six percent of participants reported no history of abortion and 24% reported one previous abortion. ART treatment history included 41.5% of participants with no history, 41.5% with one previous attempt, 10% with two previous attempts and 7% with three previous attempts. Fifty-nine percent of the participants indicated an unknown cause for their infertility, 17% indicated that the cause was related to both partners, 10% indicated a cause related to the female partner, and 14% reported a cause related to the male partner.

#### Measures

A socio-demographic questionnaire was designed to collect information concerning gender, age, social status, education level, occupation, cause of infertility, time since the beginning of pregnancy attempts, number of previous ART treatments, and number of previous abortions.

The Coping Inventory for Stressful Situations (CISS) [36] is a 48-item questionnaire that uses a Likert scale from 1 to 5 and

measures the ways people cope with stress. It was administered in the Italian validation version [37]. The questionnaire measures 3 basic dimensions: Task, Emotion, and Avoidance-oriented coping. The task scale measures the extent to which participants' cope using actions oriented to the task, planning and problem solving. The emotion scale measures whether and to what degree people use an emotional strategy to especially looking at emotional responses (getting angry, becoming tense) that in some can increase stress. The avoidance-oriented coping scale measures participants' reports of using activities and cognitive changes aimed at avoiding the stressful situation. The questionnaire showed good overall psychometric characteristics.

The Dyadic Adjustment Scale (DAS) [38-39], is a self-report questionnaire for assessing the degree of adaptation of the couple, their ways of communicating and relating by assessing the way each partner considers their relationship. It consists of thirty-two items divided into four subcategories: 1) Dyadic satisfaction (10 items) assesses the degree of satisfaction that the couples perceive within their relationship; 2) Dyadic cohesion (5 items) evaluates how much time the couple spend on pleasant activities such as social interests, dialogue and working together towards common goals; 3) Dyadic consent (13 items) is about the partners' levels of agreement or disagreement about topics like finances, spare time, religion, friends, domestic planning, and management of time spent together; 4) Emotional output (13 items) considers how the couple express their feelings, love and sexuality. The sum of these four subcategories provides a total score that expresses the general level of agreement within the couple. The questionnaire showed adequate internal reliability and good overall psychometric characteristics.

The Symptom Checklist-90-Revised (SCL-90-R) [40] is a 90-item self-report inventory which measures psychological and psychosomatic symptoms occurring in the last week. Each item is a description of a psycho-physical symptom and is rated by respondents on a five-point Likert scale (0-4) from having caused no discomfort to extreme discomfort during the past week. The SCL-90-R has 9 subscales: (1) Somatisation, (2) Obsessive-Compulsive, (3) Interpersonal Sensitivity, (4) Depression, (5) Anxiety, (6) Hostility, (7) Phobic Anxiety, (8) Paranoid Ideation and (9) Psychoticism. The sum of all 9 subscales is the Global Severity Index (GSI), which can be used as a summary of the test, reflecting overall psycho-physical distress. The SCL-90-R showed adequate test-retest reliability, internal consistency and concurrent and discriminant validity [40].

The Fertility Quality of Life (FertiQoL) [41-42] assessment is used to measure quality of life in people coping with infertility and is divided into two modules. The Core FertiQoL consists of 24 items divided into four subscales: 1) Emotional, which evaluates the impact of infertility on emotions (six items); 2) Mind-Body, which measures impacts on physical health, cognition and behaviour (six items); 3) Relational, which evaluates the impact of infertility on partnerships (six items) and 4) Social, which measures the impact on social aspects (six items). The Treatment FertiQoL is an optional 10-item module divided into two subscales: 1) Environment, which measures how patients experience the treatment environment (six items) and 2) Tolerability, which evaluates how patients are impacted by the consequences of treatment (four items). This second module was not administered in the present study since ART treatment had been suspended during the COVID-19 pandemic. Each item of the FertiQoL is scored according to 5 response categories ranging from

0 to 4. Scores are reversed, summed and scaled to range from 0 to 100. High scores on the total FertiQoL scale or any subscale indicate a better quality of life. The questionnaire showed adequate internal reliability (total and subscale Cronbach's alpha in the range of 0.72 and 0.92) and good overall psychometric characteristics [41-44].

## Procedure

This study was carried out in accordance with the code of ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. Ethical approval was granted by the Ethics Committee of the Sandro Pertini Hospital in Rome. The study was conducted between March and May 2020, during the lockdown for the COVID-19 pandemic. All medical treatments had been stopped, so the couples were informed of the study by phone. Each partner in the participating dyads was asked complete the questionnaires on an online platform after they had given their written consent. The full protocol took participants approximately forty-five minutes to complete.

## Statistical analysis

The statistical analyses were conducted using the Statistical Package for Social Science (SPSS) version 25 for Windows. Data were reported as percentages for discrete variables and as means and standard deviations for continuous variables. Pearson's correlation was used to measure the associations between fertility quality of life and coping strategies, psychophysical symptomatology and dyadic adjustment. A set of multiple linear regression analyses was performed in order to investigate the significant predictors of fertility quality of life separately for each psychological area assessed (coping strategies, psychophysical symptomatology, dyadic adjustment), with each model also including age and gender as independent variables. Further linear regression analyses were performed including the significant variables that emerged from the initial regressions. All of the variables were entered simultaneously. A  $p < 0.05$  was considered significant.

## Results

Table 1 shows participants' age, infertility duration and psychological characteristics.

Correlational analysis showed significant negative associations between the CISS Emotional scale and the FertiQoL total scale and all subscales except for the Mind-Body FertiQoL scale (Table 2). CISS Task-Orientated scale was negatively correlated with the Relational FertiQoL Scale, whereas the CISS Avoidance scale was not significantly correlated with FertiQoL (Table 2).

There were several significant correlations relating to quality of life and dyadic adjustment. Specifically, FertiQoL Emotional was positively associated with DAS Adjustment, Satisfaction and Consent scales; FertiQoL Mind-Body was positively associated with DAS Adjustment and Satisfaction scales; FertiQoL Relational was positively associated with DAS Affectivity and Satisfaction scales; and Total Core FertiQoL was positively associated with DAS Adjustment, Affectivity, Satisfaction and Consent scales. No significant findings emerged for DAS Cohesion (Table 2).

Several significant negative correlations between fertility quality of life and psychophysical symptomatology emerged (Table 3).

	Mean	sd
Age	38.62	4.39
Infertility duration (months)	36.64	27.74
FertiQoL		
Emotional	64.51	18.25
Mind-Body	72.84	17.87
Relational	83.33	16.85
Social	71.26	18.71
Total Core	72.98	12.98
CISS		
Task-oriented	54.1	6.96
Emotional	42.34	7.46
Avoidance	46	11.14
DAS		
Adjustment	125.72	9.77
Cohesion	18.31	2.72
Affectivity	10.37	1.82
Satisfaction	41.44	3.9
Consent	55.58	5.99
SCL-90-R		
Somatization	0.53	0.6
Obsessive-Compulsive	0.84	0.55
Interpersonal Sensitivity	0.55	0.55
Depression	0.71	0.68
Anxiety	0.51	0.46
Anger-Hostility	0.29	0.32
Phobic Anxiety	0.15	0.21
Paranoid ideation	0.7	0.63
Psychoticism	0.34	0.45
Global Severity Index	0.55	0.44

**Table 1:** Participants' characteristics.

FertiQoL= Fertility Quality of Life; CISS= Coping Inventory to Stressful Situations; DAS= Dyadic Adjustment Scale; SCL-90-R= Symptom Checklist-90 item Revised form

A set of multiple linear regression analyses was performed using Total Core FertiQoL scores as the dependent variable and age, gender and, separately, coping strategies and dyadic adjustment dimensions and Psychophysical Symptomatology (GSI) as predictors. The model investigating the predictive effect of coping strategies, age and gender on fertility quality of life explained 37% of the FertiQoL total scores ( $R^2=0.376$ ; adjusted  $R^2=0.240$ ), thus indicating an adequate fit of the model tested, with CISS Emotional coping as the only variable reporting a significant effect ( $\beta=0.702$ ;  $p=0.002$ ).

The model investigating the predictive effect of dyadic adjustment, age and gender on fertility quality of life produced no statistically significant findings. The model investigating the predictive effect of SCL-90 Global Severity Index, age and gender on fertility quality of life explained 28% of the FertiQoL total scores ( $R^2=0.279$ ; adjusted  $R^2=0.192$ ), with GSI having a significant effect ( $\beta=0.544$ ;  $p=0.005$ ).

Finally, the model investigating the effect on fertility quality of life of variables that had emerged as significant from the previous regressions (CISS Emotional and SCL-90 GSI) including age and gender explained 42% of the FertiQoL total scores ( $R^2=0.422$ ; adjusted  $R^2=0.326$ ), thus indicating an adequate fit of the model tested. CISS Emotional ( $\beta=-0.428$ ;  $p=0.022$ ) and SCL-90 GSI ( $\beta=-0.366$ ;  $p=0.045$ ) produced a significant effect.

## Discussion

In January of this year, the World Health Organization (WHO) declared a Public Health Emergency of International Importance due to the new Coronavirus, called COVID-19 [45], and in March COVID-19 reached the level of a pandemic due to its global geographical distribution [46]. Since then, several guidelines have been published related to reproductive medicine, and the main medical societies in this field (ESHRE, ASRM, IFFS and REDLARA-SBRA) have suggested that patients with infertility should consider deferring pregnancy [47-50]. Other common points suggestions from fertility societies worldwide included suspending initiation of reproductive treatments, including ovulation induction, Intrauterine Inseminations (IUIs), *in vitro*-fertilization, oocyte and sperm cryopreservation, and fresh/frozen embryo transfers [51].

	CISS Task	CISS Emotion	CISS Avoidance	DAS Adjustment	DAS Cohesion	DAS Affectivity	DAS Satisfaction	DAS Consent
FertiQoL Emotional	-0.040	-.562**	0.032	0.502**	-0.067	0.325	0.423*	0.474**
FertiQoL Mind- Body	-0.029	-0.192	0.001	0.409*	-0.187	0.191	0.534**	0.345
FertiQoL Relational	-0.407*	-0.409*	-0.267	0.335	-0.016	0.635**	0.373*	0.118
FertiQoL Social	0.100	-0.428*	0.196	0.337	0.108	0.235	0.168	0.320
Total FertiQoL	-0.120	-0.551**	-0.004	0.547**	-0.054	0.471*	0.514*	0.439*

**Table 2:** Association between fertility quality of life, coping strategies and dyadic adjustment.

\* $p<.05$ ; \*\* $p<.01$

FertiQoL= Fertility Quality of Life; CISS= Coping Inventory to Stressful Situations; DAS= Dyadic Adjustment Scale

	FertiQoL Emotional	FertiQoL Mind-Body	FertiQoL Relational	FertiQoL Social	Total FertiQoL
SCL-90-R: Somatization	-0.419*	-0.209	0.028	-0.230	-0.293
Obsessive-Compulsive Interpersonal	-0.386*	-0.127	-0.204	-0.376*	-0.381*
Sensitivity	-0.420*	-0.160	-0.280	-0.339	-0.416*
Depression	-.543**	-0.248	-0.334	-0.395*	-0.527**
Anxiety	-0.511**	-0.267	-0.329	-0.271	-0.476**
Anger-Hostility	-0.456*	-0.146	-0.045	-0.311	-0.337

Phobic Anxiety	-0.078	0.003	0.081	-0.084	-0.030
Paranoid ideation	-0.422*	-0.249	-0.193	-0.304	-0.406*
Psychoticism	-0.423*	-0.151	-0.298	-0.454*	-0.461*
Global Severity Index	-0.535**	-0.251	-0.288	-0.376*	-0.503**

**Table 3:** Association between fertility quality of life and psychophysical symptomatology.

\* $p < .05$ ; \*\* $p < .01$

FertiQoL= Fertility Quality of Life; SCL-90-R= Symptom Checklist-90 item Revised

The present work aimed to explore the psycho-physical well-being of infertile people forced to suspend their ART treatment for during lockdowns undertaken during the COVID-19 global health emergency. Specifically, we investigated the relationships between coping strategies, dyadic adjustment, and psychophysical symptomatology with people's quality of life related to fertility.

Results showed that quality of life was negatively related to the tendency to use emotions to manage stressful events. It is possible that, in an unexpected and uncontrollable condition, the emotional reaction is very intense and affect is unregulated. Trying to manage the stress related to the pandemic through emotional strategies therefore appears to be ineffective, leading to a lower quality of life from emotional, relational and social points of view. Also a coping style focused on planning and attempting to solve the problem appeared related to a low quality of life, specifically in the relational dimension. The literature on coping styles of infertile couples has been mixed and somewhat conflicting-some publications have highlighted the efficacy of strategies focused on activity and interactions while others have noted the efficacy of emotional avoidance. The present results should be interpreted conservatively, considering the limitations of the data collection conditions and the characteristics of our sample. In our study, people were forced to stop medical procedures, which likely led to a strong sense of impotence and helplessness. It stands to reason that attempts to act on internal and external reality in an active way were probably frustrating, which negatively impacted quality of life.

Couple relationships can be a protective factor against stress, and the results here have confirmed that those who endorsed both a greater satisfaction with their relationships and the ability to express their emotions to the partner, had a higher quality of life, not only in terms of how they perceived their relationships, but also in terms of their physical health. These results are consistent with previous literature which highlighted, independently from COVID-19 pandemic, that levels of couple's agreement, dyadic adjustment and mutual support may be understood as significant resources that can reduce the risk of reporting psychological symptoms among infertile patients undergoing medical treatments [9,24,25,27].

Additionally, we found several significant associations between fertility quality of life and psychophysical symptomatology in the couples investigated during the lockdown period. Specifically, considering only moderate to high correlations ( $r$  over .50), strong associations between general distress, depression and quality of life emerged. In general, it is known that social isolation, feelings of loneliness, fear and uncertainty for the future may increase the risk of developing psychophysical symptomatology [2]. Recent studies on general populations confirmed higher levels of depression and anxiety during the COVID-19 pandemic [52-55], specifically related

to the activation of emotional coping strategies [56]. The association between the pandemic condition, depression and a low quality of life may be more evident in an at-risk population, such as infertile people, who often are experiencing a rupture in the continuity of their identity, as well as isolation and distress.

Finally, regression analysis showed that emotional coping strategies and psychological distress specifically impact fertility quality of life, highlighting the need to support people with infertility whose care has been interrupted due to the COVID-19 pandemic. Currently, the global pandemic is worsening and several countries are again activating social protection measures, including isolation at different levels. We do not know if we will still have to face a period of lockdown and interruption of ART treatments, but the results of this research offer important considerations for planning alternative psychological support activities in case that occurs. For example, psychological support through telemedicine could serve as an important tool for ART specialists. During the lockdowns, several digital platforms quickly proved valuable in allowing for communication and relationship maintenance among patients, physicians and psychologists. Most fertility organizations expressly recommended the use of such tools during the pandemic; what the present study adds is a specific focal point of that intervention-attending to coping strategies during lockdowns and care interruption in addition to management of psychopathological symptoms.

There are several limitations that characterize this study. First is the small sample size. The study was conducted through online platforms, but less than half of the patients who were invited to participate did so. This phenomenon could be explained by the sense of indignation and helplessness that people may have felt when faced with the need to interrupt treatment or not start it when they had planned, especially considering that the study was conducted in a public ART center, where waiting lists can be quite long. The interruption for some couples therefore prolonged an already difficult wait; for some it may have brought the couple beyond the age limit established by the law in Italy for utilizing reproductive medicine. No guidelines were immediately available for the management of patients with infertility during ART, and probably the sense of isolation and lack of support negatively impacted some people's motivation to participate in the study. Another limitation is represented by the online administration, which does not guarantee an adequate setting for the use of psychological measures. This was an unavoidable issue in the present study, but conducting such research during the process of online or virtual patient care in the future might help to make the process more reliable. The cross-sectional nature of the study also did not allow for causal inferences in the relationships between the observed variables. It would be interesting to observe the patients longitudinally, to assess their long-term psychophysical health and the impact of the lockdown and related interruptions of ART on the outcomes of the treatments themselves, once resumed.

## Conclusion

Despite these limitations, the findings of the present study showed several associations between fertility quality of life and coping strategies, psychophysical symptomatology and couple relationship dimensions. Therefore, health professionals working in this context during this difficult period should focus their intervention on the marital relationship, particularly on the issue of mutual support between partners, since promoting mutual support and care seem to protect partners from possible negative consequences of treatment suspension. Moreover, it also may be important to promote functional coping strategies in order to reduce the negative effect on quality of life and well-being.

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## Conflict of Interest

The authors declare that they have no conflict of interest.

## Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Ethical approval was granted by the Ethics Committee of the Department of Dynamic and Clinical Psychology of the University of Roma "Sapienza".

## Informed Consent

Informed consent was obtained from all individual participants included in the study.

## Data Accessibility Statement

Data supporting the results showed in the paper will be available from the corresponding author on request.

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