



Review Article

SCIENTIFIC STUDIES ON THE EFFECTS OF THE CHANGES IN TREATMENT PROCESSES DURING THE COVID-19 PANDEMIC ON INFERTILE COUPLES: LITERATURE REVIEW

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Abstract: *The COVID-19 pandemic has been rapidly raging. Suspending the services related to infertility and assisted reproductive techniques are among the measures taken to prevent the spread of the epidemic. Various guides and recommendations have been published by many national and international associations for this purpose. Recommendations foresee the completion of cycles that have already been initiated and require no new reproductive therapies to be initiated except for patients with a low ovarian reserve and those with a background of oncological disorders. The majority of couples whose treatment is suspended/postponed throughout this process have experienced intense stress, sadness, and anxiety. In addition, some of the patients do not have adequate coping skills. This article is designated as a literature review in order to provide information about the current emotional states of infertile couples throughout the COVID-19 pandemic and to guide the studies planned for their needs. Due to the fact that the subject is related to the pandemic, the years covered by the literature review were limited to 2019 and later. As a result of the literature review; 2 studies conducted in Turkey and 5 studies conducted abroad, examining the effects of COVID-19 on infertile couples, were included. The majority of studies revealed that suspending fertility treatments caused high levels of anxiety and stress in infertile couples. Providing psychological counseling services to couples through online platforms by health professionals is thought to enable couples to cope better with the situation.*

Keywords: *COVID-19, infertility, anxiety, stress, fertility treatment.*

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1. Introduction

COVID-19 was initially reported in December 2019 in Wuhan (China); subsequently, the epidemic raged rapidly in other parts of the country. With the spread of the epidemic to other countries in a short time, COVID-19 disease was declared a pandemic by the World Health Organization (WHO) on March 11, 2020, when the first case was observed in Turkey [1,2]. A series of recommendations have been published on issues such as reorganizing hospital staff and resources as well as clinic and patient management in accordance with the need to take the necessary precautions to use the health system effectively during the COVID-19 pandemic. For this reason, associations and regulatory authorities operating on reproductive health have published guidelines based on expert suggestions and offered various recommendations in order to prevent a possible collapse in the health system during the pandemic. Organizations such as the European Society of Human Reproductive and Embryology

(ESHRE), the American Society of Reproductive Medicine (ASRM), The Fertility Society of Australia (FSA), and the Turkish Society of Reproductive Medicine (TSRM) suggested suspending the acceptance of new pregnancy cycles and to postpone the beginning of new treatment cycles except for the patients currently on their gestation cycle or requiring immediate fertility preservation due to ongoing cancer treatment. [3-7] In this context, the Ministry of Health of the Republic of Turkey decided to suspend new elective procedures and treatments in line with the recommendations of national and global health associations on the grounds of a circular published on March 17, 2020 [8]. Unexpected closures of fertility clinics both around the world and in Turkey have hindered the dreams of infertile couples to have a baby that they have been longing for years. Furthermore, the uncertainty about the pandemic outbreak may cause disappointment in these groups, who are already easily vulnerable and aggravate their anxiety and hopelessness about the success of the treatment process. This article is designated as a literature review in order to provide information about the current emotional states of infertile couples throughout the COVID-19 pandemic and to guide the studies planned for their needs.

2. Material and Method

Due to the fact that the subject is related to the pandemic, the years covered by the literature review were limited to 2019 and later. Electronic databases such as Pub-Med, Science Direct, Ebsco Host, Ovid, CINAHL have been scanned using the keywords 'covid-19, infertility, anxiety', 'covid-19, fertility treatment, postponement', 'covid-19, infertility, stress and coping'. The study included factors that negatively affect the emotional state of infertile couples whose fertility treatment was postponed, which were determined in the light of the studies examined, as well as related cross-sectional studies. As a result of the literature review; a total of 7 research studies, examining the effects of COVID-19 on infertile couples, were examined. 2 of these studies were conducted in Turkey while 5 of them were conducted abroad.

3. Results and Conclusion

The Covid-19 pandemic; which has already caused great stress all over the world and still has many unknowns, including its duration and health effects, is likely to have negative effects on infertile individuals who are among the vulnerable groups. Many studies have revealed that the closure of fertility clinics due to the pandemic creates intense stress, anxiety, and sadness in couples (Table 1). Ben- Kimhy et al. (2020) revealed in their study that patients whose treatments were suddenly suspended due to the Covid-19 pandemic felt very helpless, stressed, and lonely. In addition, it was determined that the stated stress level aggravated in relation to elderly ages and being alone. It has also been argued that patients with adequate social support systems are less affected by this process; hence it is necessary to strengthen these systems, which play an important protective role in times of crisis and help reduce distress levels. In addition, it has been stated that access to social support systems has become more challenging and may be associated with stress, with the force of the social distance applied during the pandemic period. Therefore, it has been suggested that online support groups may be an effective intervention to address the perceived need for socialization during periods of limited social interaction such as quarantine. In addition, it has been noted that encouraging patients to engage in activities such as doing exercise and healthy nutrition to optimize success after re-initiating treatments may provide patients a meaningful goal during quarantine. It has been argued that it is very important to communicate with patients during this period, which is defined as a psychologically distressing situation, and to provide psychosocial counseling when needed. It was stated that caregivers could use the data identified to identify the patients at higher risk of emotional distress and to adjust policies regarding the suspension of treatment in current and future events [9].

Barra et al. (2020) found that there was a significant increase in the stress, anxiety, and depression levels of couples whose treatment was either suspended or postponed due to the Covid-19 pandemic. It has been stated that these psychological outcomes are significantly more challenging in women over the age of 35 and who have attempted IVF before and that the occurrence of psychological symptoms is significantly related to the time exposure to news about Covid-19. In addition, other reasons for the increased incidence of psychological symptoms in women have been shown to be inadequate ovarian reserves, endometriosis, and uterine fibroids. The study further underlined that not only women but also men undergoing infertility treatment experience anxiety and stress and it was emphasized that the psychological consequences of suspending andrological services during quarantine should be taken into account. It was suggested that psychological counseling services should be strengthened in order to reduce psychological distress, improve the mental health and quality of life of patients who have applied to IVF centers throughout the Covid-19 outbreak. It was suggested that specific strategies could be developed for this purpose and these strategies could be notified to patients systematically during the treatment through various methods (i.e. brochures, websites, personal referrals) and via multiple providers (i.e. psychologists, doctors, medical assistants, nurses) [10].

Esposito et al. (2020) have stated in their study that the existence of the current Covid-19 pandemic and the suspended ART programs thereto caused stress in infertile couples. It has been determined that the unknown effect of Covid-19 on the fetus causes anxiety in infertile couples. However, the majority of couples were found to be willing to continue ART programs despite the existing unknowns. In addition, while the percentage of uncertainty about pregnancy safety was found to be significantly higher in patients with a shorter infertility period, it was determined that patients with infertility for more than 1 year were more likely to take risks and resume the program to get pregnant. This issue may be included within the considerations of resumption of programs because many centers have already been prioritized for couples of elder maternal ages or couples who are close to the government-determined threshold for taking infertility ART services in terms of waiting lists. Infertile couples with individuals who were affected by Covid-19 in their family or environment had higher levels of anxiety compared to those who did not. It has further been determined that some infertile couples plan to give up ART programs due to the economic crisis caused by the pandemic. In general, it has been underlined that the psychological consequences of the Covid-19 pandemic on infertile patients should not be underestimated and specific psychological support should be planned [11].

The research studies conducted by Boivin et al. (2020) revealed that the closure of infertility clinics had adverse effects on patients which may be considered extreme, uncontrollable, and stressful. The current situation was perceived as a threat to the achievement of patients' goals of becoming parents. The majority of the patients were able to cope with the uncertainty of the situation by using various strategies (distraction, focusing on the positive aspects, adapting mentally and physically for subsequent treatments, strengthening their social networks, and staying up to date). On the other hand, it has been reported that 11,9% of women consider methods such as avoidance and denial and do not attain the necessary resources to cope effectively. It was further argued that being well informed about the psychosocial vulnerabilities of the patients related to infertility appeared to be important, particularly during the current crisis. Therefore, it has been emphasized that various strategies can be developed to monitor the weakened mental health associated with infertility treatment during the Covid-19 period. It was further suggested that the relevant authorities should work in collaboration and proactively manage the process to address the uncertainty arising from the pandemic outbreak. Moreover, it has been suggested that future psychological studies aiming to support patients' coping strategies should prioritize identifying patients at risk of distress with standard measures and develop digital technologies that are appropriate to the realities of fertility care in the context of Covid-19 [12].

Turocy et al. (2020) discussed in their study that 85% of the patients whose cycle was suspended find this situation moderate to extremely distressing, while 22% perceive this situation as equivalent to the loss of a baby. It was determined that the rate of patients not agreeing with the suspension of their cycles, in line with American Society for Reproductive Medicine (ASRM) recommendations was higher than the rate of agreement. In addition, the majority of the patients whose cycles were suspended stated that they wanted to resume their treatment in consultation with their doctor. It was stated that the majority of patients agreed with the opinion that diagnostic procedures such as hysterosalpingogram, hysteroscopy, and laparoscopy should be canceled. The study argued that patients' feedback on ASRM guidelines may be used to shape health policies to be developed for the pandemic period [13].

Tokgöz et al. (2020) revealed that the prevalence of state anxiety is higher in women whose ART cycles were delayed due to the Covid-19 outbreak. In addition, women with reduced ovarian reserve were found to have higher anxiety levels. It has been stated that women who believe that the possibility of not getting pregnant is more important than the risk of being infected with COVID-19 have a higher level of anxiety compared to women who have the opposite opinion. It has been suggested that support and intervention studies for infertile women should be focused on improving negative emotional factors [14].

Arbağ et al. (2021) discussed in their study that the vast majority of women who received infertility treatment felt helpless, sad, worried, and angry due to changes in their treatment programs, they experienced uncertainty and were tired of waiting. They also stated that the stress experienced by women due to infertility problems is much higher than the fear of being infected with COVID-19. The majority of women also stated that their spouses supported the suspension of their treatment during the pandemic outbreak. Some women stated that they did not agree with their husbands on this issue. For this reason, it has been argued that the level of anxiety and stress experienced due to the suspension of infertility treatment is higher in women compared to men. In addition, some women did not find the decision to postpone the treatment reasonable and asserted that this was applied to protect the health personnel from infection. Therefore, women experienced feelings of anger, distrust, and threat toward health officials. On the other hand; it has been stated that there are female patients who feel themselves safe, hence welcoming the suspension of the treatments due to the uncertainty of the pandemic and its potential adverse effects on both the pregnancy and the baby. It has been determined that the psychological changes experienced by women suffering from infertility problems due to the pandemic cause a decrease in their self-esteem and aggravate negative changes in their body images. The women stated that they would resume their treatment despite the financial difficulties experienced due to the pandemic. The women in question said that they resorted to coping methods such as praying, exercising, distracting, meditating, and drawing attention to the positive aspects of the suspension of infertility treatment during the pandemic process. On the other hand, it was determined that non-functional coping methods (crying, rebelling, blaming health authorities) also resorted among women with insufficient coping resources. For this reason, the importance of evaluating women's coping methods and empowering women who are inadequate in this regard was emphasized. According to these evaluations, it was stated that nurses may be assigned to support patients on various issues through online platforms. In addition, it was suggested that online peer support programs aiming to strengthen social support could be implemented and women's coping skills could be improved by organizing training to develop effective coping strategies [15].

Table 1. Summary of prior studies on the effects of Covid-19 on infertile couples

Item No	Author(s)	Publishing Journal	Title-Purpose of the Article	Method	Results
1	Ben-Kimhy et al. 2020	Human Reproduction	<p>Title: Fertility patients under COVID-19: Attitudes, Perceptions, and Psychological Reactions</p> <p>Purpose: To examine the factors associated with the perceptions, attitudes, and psychological distress of infertile patients whose treatment was suspended during the Covid-19 process.</p>	<p>Place of Research: Israel</p> <p>Type of Research: Cross-sectional Study/online survey</p> <p>n:168</p>	<ul style="list-style-type: none"> * Despite the decision executed by the Ministry of Health, 72% of the patients reported during the survey that they wanted to resume their treatment. * The patients stated that they felt very helpless, stressed, and lonely. * It was stated that elder age and being alone were associated with higher levels of distress and stress for patients. * It has also been argued that patients with adequate social support systems are less affected by this process.
2	Barra et al. 2020	Journal of Psychosomatic Obstetrics & Gynecology	<p>Title: Psychological status of infertile patients who had in vitro fertilization treatment interrupted or postponed due to COVID-19 pandemic: a cross-sectional study.</p> <p>Purpose: To investigate the psychological state of infertile women and men whose in vitro fertilization (IVF) treatment was interrupted or postponed due to the Covid-19 emergency.</p>	<p>Place of Research: Italy/Genoa</p> <p>Type of Research: Cross-sectional Study/online survey</p> <p>n:524</p>	<ul style="list-style-type: none"> * The prevalence of feelings of anxiety and/or depression was found to be significantly higher, especially in women older than 35 years of age and who had previously attempted IVF. * The occurrence of psychological symptoms is found to be significantly related to the time of exposure to news about Covid-19. * It has been determined that women with low ovarian reserves, suffering endometriosis and uterine fibroids more frequently indicate psychological symptoms. * Women with infertility factors are found to exhibit higher anxiety and/or depression status compared to those without; similarly, it was found that male patients with infertility factors are more likely to exhibit anxiety and/or depression frequently compared to those without. * While 196 individuals participating in the study stated that they wanted to resume IVF treatment despite the Covid-19 pandemic, 401 individuals stated that the opportunity to know when they could resume their IVF treatment would make them feel safer.

Table 1 continued.

Item No	Author(s)	Publishing Journal	Title-Purpose of the Article	Method	Results
3	Esposito et al. 2020	European Journal of Obstetrics & Gynecology and Reproductive Biology	Title: Influence of COVID-19 pandemic on the psychological status of infertile couples Purpose: To evaluate the impact of the Covid-19 pandemic on the emotions, concerns, and future plans of infertile couples.	Place of Research: Italy Type of Research: Online survey n: 627	<ul style="list-style-type: none"> * The Covid-19 pandemic and subsequent suspension of ART programs have led to increased stress levels in infertile couples. * The uncertainty of the effect of Covid-19 on the fetus is found out to aggravate the level of anxiety in couples. Despite this, 64.6% of the participants stated that they wanted ART programs to be resumed. * It has further been determined that 11.5% of the infertile couples plan to give up ART programs due to the economic crisis caused by the pandemic. * Couples with at least one relative affected by the Covid-19 outbreak have been found to experience higher levels of anxiety compared to unaffected families.
4	Boivin et al. 2020	Human Reproduction	Title: Patient experiences of fertility clinic closure during the COVID-19 pandemic: appraisals, coping, and emotions Purpose: To evaluate the reactions of patients towards the closure of infertility clinics due to Covid-19; to examine coping strategies and emotional responses.	Place of Research: United Kingdom Type of Research: Mixed Method/Cross-Sectional Study n: 450	<ul style="list-style-type: none"> * Almost all patients reported stress, anxiety, and frustration about the situation; while others expressed that they felt anger and resentment towards the injustice of the situation. * It was stated that the closure of infertility clinics had a negative effect on the lives of the patients rather than a positive one. * The uncertainty created by the situation was perceived by the patients as a threat to the achievement of the goal of having a baby. * Majority of the patients were able to cope with the uncertainty of the situation by using various strategies (distraction, focusing on the positive aspects, adapting mentally and physically for subsequent treatments, strengthening their social networks, and staying up to date).

Table 1 continued.

Item No	Author(s)	Publishing Journal	Title-Purpose of the Article	Method	Results
5	Turocy et al.2020	Fertility and Sterility	<p>Title: The Emotional Impact of the ASRM Guidelines on Fertility Patients During the COVID-19 Pandemic</p> <p>Purpose: To investigate the opinions of patients undergoing fertility treatment during the COVID-19 pandemic about ASRM recommendations and the emotional effects these recommendations have had on patients.</p>	<p>Place of Research: United States</p> <p>Type of Research: Online survey</p> <p>n: 518</p>	<ul style="list-style-type: none"> * 85% of patients whose cycle was canceled reported that they found this situation moderate to extremely distressing. * As a matter of fact some reported that they perceive this situation as equivalent to the loss of a baby. * It was determined that the rate of patients not agreeing with the suspension of their cycles, in line with American Society for Reproductive Medicine (ASRM) recommendations was higher than the rate of agreement. * Majority of the patients whose cycles were suspended stated that they wanted to resume their treatment in consultation with their doctor.
6	Tokgoz, Kaya, Tekin. 2020	Journal of Psychosomatic Obstetrics & Gynecology	<p>Title: The level of anxiety in infertile women whose ART cycles are postponed due to the COVID-19 outbreak</p> <p>Purpose: To evaluate the level of fear and anxiety about the Covid-19 outbreak in infertile women whose ART cycles were delayed due to the pandemic.</p>	<p>Place of Research: Turkey</p> <p>Type of Research: Cross-sectional Study/online survey</p> <p>n: 101</p>	<ul style="list-style-type: none"> * The level of state anxiety was found to be higher in women whose treatments were delayed due to the epidemic. * The decrease in ovarian reserves was found to significantly affect anxiety levels. * It has been concluded that worrying about not being able to have children causes higher levels of anxiety than being infected with the coronavirus.

Table 1 continued.

Item No	Author(s)	Publishing Journal	Title-Purpose of the Article	Method	Results
7	Arbağ, Aluş Tokat, Fata. 2021	ESHRE's 37th virtual Annual Meeting 2021	<p>Title: Emotions, Thoughts, and Coping Strategies of Women with Infertility Problems on Changes in Treatment during Covid-19 Pandemic: A Qualitative Study</p> <p>Purpose: Using Folkman's Transactional Stress and Coping Model to evaluate the feelings, thoughts, and coping strategies of women patients suffering infertility regarding treatment changes throughout the Covid-19 pandemic.</p>	<p>Place of Research: Turkey</p> <p>Type of Research: Qualitative Study</p> <p>n: 30</p>	<p>* Some women perceived the changes in treatment programs positively and stated that suspending the treatment made them feel safer due to the uncertainty created by the pandemic and the yet unpredictable effects of the virus on the pregnancy process and the baby.</p> <p>* Majority of the women evaluated that the closure of their clinics had a negative impact on their lives.</p> <p>* They reported that they experienced hopelessness, uncertainty, disappointment, anxiety, anger, sadness, and exhaustion during this process.</p> <p>* Women perceived changes in infertility treatments as a stronger stressor than coronavirus.</p> <p>* In addition, some women did not find the decision to postpone the treatment reasonable and asserted that this was applied to protect the health personnel from infection.</p> <p>* Women experienced feelings of anger, distrust, and threat towards health officials.</p> <p>* Moreover, women stated that they had to stay at home all the time throughout the pandemic, they had to stay away from their friends and families, therefore they did not need self-care hence saw themselves as uglier.</p> <p>* The women stated that they would resume their treatment despite the financial difficulties experienced due to the pandemic.</p> <p>* The women in question said that they resorted to coping methods such as praying, exercising, distracting, meditating, and drawing attention to the positive aspects of the suspension of infertility treatment during the pandemic process.</p>

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The Declaration of Ethics Committee Approval

The author declares that this document does not require an ethics committee approval or any special permission. Our study does not cause any harm to the environment.

Compliance with Research and Publication Ethics: This work was carried out by obeying research and ethics rules.

Authors' Contributions:

YDO: reviewed literature, wrote, and revised the manuscript. SD: provided assistance and reviewed and revised the manuscript.

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