



Parenthood in Infertile Couples Attending Assisted Reproductive Technologies (ARTs) Centers: What Has Changed During the COVID-19 Pandemic?

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Abstract

Background: The COVID-19 pandemic has been shown to impact the lifestyle of couples of reproductive age and, in particular, their desire for parenthood. The purpose of this study was to carry out an evaluation on the potential changes of desire for parenthood among infertile couples waiting for assisted reproduction during the pandemic.

Methods: In this multicenter cross-sectional study, the quality of sexual life in Italian infertile couples was assessed and their well-being was evaluated before the pandemic and during the quarantine. All couples were asked to fill out a questionnaire, in which their desire for parenthood, sexual life, and well-being were investigated.

Results: Out of 1650 cases, 300 patients were finally enrolled. COVID-19 negatively impacted the well-being of individuals, leading to significantly reduced scores of happiness, feeling energetic, and interest in life ($p < 0.05$). Although most couples had prolonged infertility, a small number of cases (4.0%) achieved a spontaneous natural pregnancy during the lockdown, probably due to more intimacy and longer time spent together. However, major concerns about the consequential effects of the virus on pregnancy and the risk of contagion in the hospital led a small number of infertile couples (5.0%) to decide to postpone their parenting project.

Conclusion: The COVID-19 pandemic may have created a further negative impact on couples, reducing their desire for parenthood. This attitude could result in a decrease in births in the near future.

Keywords: COVID-19, Life style, Parents, Patients, Quality of life, Reproduction.

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Introduction

By the end of 2019, a novel type of Coronavirus, known as SARS-CoV-2, has rapidly circulated among humans, developing a glo-

bal outbreak. The signs and symptoms of the viral infection are consistent with a disease called Coronavirus Disease 2019 (COVID-19), character-

ized by acute bilateral interstitial pneumonia and severe acute respiratory syndrome, which may lead to death in a short period of time. On March 11 th, 2020, the Director-General of the World Health Organization (WHO) formerly declared COVID-19 as a global pandemic, which is currently ongoing (1).

Although COVID-19 emerged in China, the infection rapidly expanded in the world, involving several countries including Italy, that was one of the first western countries to be significantly impacted. Consequently, similar to the majority of countries, Italy adopted a combination of containment and mitigation measures in order to reduce the spread of the infection (2). The strongest measure was represented by the lockdown, lasted from the 9th of March 2020 to the 1st of May 2020.

This war-like sanitary emergency had numerous effects on society, families, and couples, posing a challenge to the psychological resilience (3). Although until then, there was no scientific evidence that female or male genital tracts can be directly influenced by SARS-CoV-2 (4), on March 17 th, 2020, the public authorities for Assisted Reproductive Technology (ART) in Italy, namely National Center of Transplants (CNT) and Istituto Superiore di Sanità (ISS), delivered their prevention measures for SARS-CoV-2 transmission in reproductive cells and ART treatments (5). These institutions recommended to avoid non-urgent gamete donation programs, suspending in-vitro fertilization (IVF) protocols and office activity for couples who have not yet started ovarian stimulation, except for urgent treatments (*i.e.* fertility preservation for cancer).

This situation increased the anxiety and worries in Italian couples waiting for IVF treatments. A recent study evaluated the impact of the COVID-19 pandemic on the lifestyle in Italian couples of reproductive age and, in particular, on their desire for parenthood. The researchers reported that from the sample of participants who were planning to have a child before the pandemic, 37.3% abandoned the intention due to worries of future economic difficulties and consequences of pregnancy. Nevertheless, a considerable number of couples who were planning for childbearing before the pandemic continued their attempts, and similarly some couples started to express their reproductive desire exactly during the quarantine. In this scenario, sexual life and desire for parenting have been significantly influenced by the awareness of living

during a dangerous era (5, 6). Some studies have evaluated the changes due to the closure of the centers for medically assisted procreation during the period of the pandemic (7) and others have highlighted the emotional sufferings of couples (8-10); still others evaluated the change in desire for parenthood during the period (6) and spontaneous pregnancies among infertile couples during assisted reproduction lockdown in COVID-19 pandemic (11).

The primary goal of this research was then to fill this gap by carrying out an evidence-based study on the potential changes of desire for parenthood in couples awaiting for homologous or heterologous IVF procedures. Moreover, the alterations in mental well-being of couples were evaluated and the quality of their sexual life was assessed before the pandemic and during the quarantine.

Methods

A multicenter cross-sectional observational study was conducted two months after the beginning of the national lockdown, from first of April, 2020 to first of May, 2020, in various private and public sectors that deal with ARTs in Tuscany (Italy). All the couples attending an ART center for infertility were asked to fill out a questionnaire, in which their desire for parenthood was investigated.

The questions were written in Italian language to evaluate the impact of COVID-19-related control measures on couples' reproductive desire and on the individuals' mindset and their quality of life. The study involved the creation of a web-based survey including 25 items in total, designed in Italian version, in accordance with the Checklist for Reporting Results of Internet E-Surveys (CHERRIES). All the potential participants were fully informed about the study, degree of privacy, anonymity and confidentiality, possible risks and benefits, the voluntary nature of participation, and the lack of negative consequences in case of decline. All the patients enrolled gave their consent to participate, according to ethical principles of the Declaration of Helsinki and based on the study's Ethics Committee (Care Covid-19 AOUC Project) approval. A disclosure was fixed on the first sheet of the online survey, in which participants were required to check a box to indicate consent before accessing the survey. The questionnaire was developed through the use of Google Forms and distributed by email.

Based on the inclusion criteria, the following

couples were selected: (1) couples who had already performed a first consultation, but who were waiting for IVF/ICSI cycle and temporarily "suspended" after the start of the pandemic; and (2) couples who had already performed one or more IVF/ICSI cycles, waiting for another cycle and temporarily "suspended" after the start of the pandemic.

Couples and/or single individuals who did not complete the questionnaire and couples and/or single individuals who completed the questionnaire after the first of May, 2020 (date of conclusion of the study) were excluded.

Data collection: Patients' demographic data including gender, age, and level of education were recorded. Participants were asked whether they had positive test results for SARS-CoV-2. Information about the marital status, previous children, and their presence at home during the quarantine, as well as the average time spent per day with the partner at home was collected.

Duration of couple infertility, cause of infertility, type of ARTs program planned, previous IVF/ICSI cycles, and natural pregnancy achieved during the lockdown period were checked.

Sexual behaviors were analyzed, collecting the median value of sexual intercourse per week before and during the pandemic. Also, the continuation of unprotected sex for the purpose of conception was reported.

Socio-economic issues were explored including the need to leave home due to work commitment and the mean difference of monthly profits during and before the pandemic was compared. Patients were asked about the changes in their desire for parenthood during the quarantine period and also potential reasons for occurrence of such feelings were investigated. In particular, couples were asked whether they continued to desire having a child or decided to temporarily/definitively give up the intention. Therefore, patients who stopped the plan were asked to provide the reasons why the changes might have occurred, being able to choose more than one option among the answers. Moreover, patients who decided to stop unprotected sex for purpose of conception were asked the potential reasons which led to this choice.

The evaluation of different outcomes between genders was also done. Desire for parenthood domains was also analyzed by stratification of the study population into age groups. The mood of participants before the beginning of the COVID-

19 pandemic and during the quarantine was assessed, using a validated WHO questionnaire, the Well-Being Index (1998 version). Two different periods including the last two weeks of the pre-pandemic period and the lockdown period were compared, asking the study participants how they felt in the previous two weeks. In the current study, which ended on the first of May, people's well-being during the lockdown, in a period that preceded the conclusion of the lockdown period in Italy by two weeks, was investigated. The sub-heading of the questionnaire consisted of five statements which were related to how the patient was feeling over the last two weeks before the pandemic and during the last two weeks of the lockdown, taking into account that higher numbers mean better well-being. For each statement, a value from 0 (at no time) to 5 (all of the time) was allocated. The raw score was calculated by totaling the values of the five answers. The raw score ranged from 0 to 25 for which 0 represented the worst possible and 25 represented the best possible quality of life.

Statistical analysis: Continuous variables are presented as median and interquartile range (IQR) and were compared by the student independent t-test or the Mann-Whitney U test based on their normal or non-normal distribution, respectively (normality of variables' distribution was tested by the Kolmogorov Smirnov test). Categorical variables were tested with the Chi-square test. All statistical analyses were completed using SPSS v17.0 (IBM, US). For all statistical comparisons, a significance level of $p < 0.05$ was considered to show differences between the groups using Wilcoxon signed rank test.

Results

Out of 1650 people invited for participation, 300 patients finally filled out the questionnaire (response rate=18.2%). Overall, 126 men (42.0%) and 174 women (58.0%) were included in the study. The median of patients' age was 39.0 (IQR: 35.0-43.0) years old. The median of male age was 41.0 (IQR: 36.0-45.0) and median of female age was 37.0 (34.0-41.0). Demographic data are shown in table 1. The most represented level of school education was tertiary (41.3%). A total of 292 participants (97.3%) lived in the same place with the partner during the quarantine, and 269 (90.0%) spent more than 12 *hr* a day at home with their partners.

Table 1. Demographic and socio-economic data of participants (n=300)

Variables	Value n (%)
Level of education	
Secondary school	54 (18.0)
Post-secondary school	122 (40.7)
Tertiary (graduation)	124 (41.3)
Previous children, n	
No	260 (86.7)
Yes	40 (13.3)
COVID-19 diagnosis	
No	287 (95.7)
Yes	13 (4.3)
Quarantine at home with the partner	
No	8 (2.7)
Yes	292 (97.3)
Time spent with the partner at home (hr)	
0	5 (1.7)
<12	25 (8.3)
>12	66 (22.1)
>18	48 (16.1)
24	155 (51.8)
Active work outside during quarantine	
No	202 (67.3)
Yes	98 (32.7)
Reduction of monthly profits during quarantine	
Unchanged	147 (49.0)
1-20% less	45 (15.0)
21-50% less	49 (16.3)
51-70% less	29 (9.7)
71-100% less	30 (10.0)
Type of ART centers	
Private	19 (6.3)
Private agreement	10 (3.3)
Public	271 (90.3)
Duration of couple infertility	
>1 year	47 (15.7)
>2 years	78 (26.0)
>3 years	72 (24.0)
>4 years	103 (34.3)
Marital status (married)	
No	126 (42.0)
Yes	174 (58.0)
Types of planned ART program	
Homologous	113 (37.3)
Heterologous	145 (48.3)
Not planned yet	42 (14.0)
Causes of infertility	
Male factor	61 (20.3)
Female factor	144 (48.0)
Both	25 (8.3)
Unknown	70 (23.3)
Previous IVF/ICSI cycles	
No	189 (63.0)
Yes	111 (37.0)
Natural pregnancy during the quarantine	
No	288 (96.0)
Yes	12 (4.0)

ART= Assisted Reproduction Technology, IVF=In vitro fertilization, ICSI= Intracytoplasmic Sperm

Table 2. Sexual behaviors before and during the COVID-19 pandemic

Question	Before COVID-19	During COVID-19	p-value
Sexual intercourses per week			
0	6 (2.0)	28 (9.3)	0.28
1	103 (34.3)	93 (31.0)	
2-4	181 (60.3)	160 (53.3)	
>4	10 (3.3)	19 (6.3)	

All values are expressed in n (%). A significance level of $p < 0.05$ was considered to show differences between the groups using Wilcoxon signed rank test

The majority of people (84.3%) had infertility duration of longer than 2 years and 260 patients (86.7%) had history of primary infertility.

As table 2 shows, the median value of sexual intercourse per week did not differ significantly before and during the pandemic ($p=0.28$). Among 245 couples (81.7%) who continued to attempt unprotected sexual intercourse for conception during the quarantine, 12 (4%) cases achieved spontaneous natural pregnancy during this period.

Concerning the desire for parenthood, 15 participants (5.0%) temporarily desisted from their intention to conceive. The main reasons that led people to this decision included worries about potential viral effects on pregnancy (40%) and possibility of contagion in hospital settings (33%). Fear for future economic difficulties (26.7%) and couples conflicts (13.3%) were the other possible motives that culminated in termination of couples' plan. Among the rest of couples, the main reason for termination of plan (50.0%) was the increased anxiety of couples' regarding their current situation who have stopped unprotected sex despite not having suspended the desire for parenthood.

Changes in the desire for parenthood during the quarantine period did not differ significantly between genders ($p=0.36$), nor between age groups ($p=0.70$). Moreover, younger patients (<39 years) continued their attempts for conception more than older ones ($p=0.03$).

Although no significant differences were reported between changes in desire for parenthood and duration of infertility, most couples who decided to desist from the intention to conceive had history of infertility of lesser duration (8.5% vs. 3.9% comparing >1-year vs. >4-year).

No relationship was found between changes in desire for parenthood and cause of infertility ($p=0.11$), nor type of planned ARTs (*i.e.* homo-

Table 3. Well-Being Index subdomain values before and during the COVID-19 pandemic

	Median (IQR)		p-value
	Before COVID-19	During COVID-19	
I have felt calm and relaxed	3.0 (3.0-4.0)	3.0 (2.0-4.0)	0.11
I have felt active and vigorous	4.0 (3.0-4.0)	3.0 (2.0-4.0)	<0.01
I have felt cheerful and I am in good spirits	4.0 (3.0-4.0)	3.0 (2.0-4.0)	<0.01
I have felt cheerful and I am in good spirits	3.0 (2.0-4.0)	4.0 (2.0-4.0)	0.8
My daily life has been filled with things that interest me	4.0 (3.0-4.0)	3.0 (2.0-4.0)	<0.01

Continuous variables are presented as median and interquartile range (IQR). A significance level of $p < 0.05$ was considered to show differences between the groups using Wilcoxon signed rank test

gous or heterologous program) ($p=0.34$).

Total median value for Well-Being Index before COVID-19 pandemic was significantly higher compared to the value during the pandemic period (17.0 vs. 16.0, $p < 0.01$). In particular, significant differences in median values before and during the pandemic period were reported in the subdomains regarding feelings of happiness, feeling energetic, and interest in life (Table 3).

Discussion

The purpose of the current research was to introduce better strategies to deal with this emergency condition for reducing the psychological impact of anxiety, depression, and stress of individuals and couples. At the beginning of the pandemic, it could have been hypothesized that slow life rhythm during the quarantine could have led to improvements in couple intimacy and the number of sexual intercourses, likely resulting in a rise in birth rates.

Indeed, since couple's life is upset by the hectic pace of everyday routine, the increased time spent together could have led to an improvement in marital satisfaction. In our case series, the median value of sexual intercourse did not change significantly during the lockdown, but some differences in the two extreme subgroups were observed (the lowest (0) and highest frequency (>4) of sexual intercourse per week). The frequency of "zero" answer ranged from 2.0% to 9.3% and the " >4 " answer from 3.3% to 6.3%.

Other researchers provided different conclusions; reduced sexual relations and augmented autoerotism take place during the pandemic period in couples of reproductive ages (14, 15). This discrepancy could be probably related to different perceptions of sexuality; infertile couples who attend ARTs centers look primarily for procre-

ation, whereas the other ones look for pleasure and intimacy.

As demonstrated in literature, the pandemic may have negatively impacted the psychological well-being of individuals (16). Likewise, psychosocial factors such as depression symptoms, anxiety, distress, and unhealthy lifestyle could be linked to reduced chances of natural pregnancy (17, 20). In our study, total median of Well-Being Index was significantly higher before the COVID-19 pandemic, in particular, with regard to the subdomains of happiness, feeling energetic, and interest in life. However, relaxation (relaxed) domain was similar before and during the pandemic. In fact, this state of mind could not be directly related to external situations, whereas recovery (restored) domain was better during the period in comparison to the time before the lockdown, as this item is usually influenced by slow and restful rhythms of life. However, it is possible to hypothesize that asking to recall past emotions can be subject to significant distortion due to memory errors, as well as the fact that the negative impact of COVID may be overestimated by participants.

In this study, 90.0% of the patients spent more than 12 hr a day at home with their partners. The longer available time spent together might have contributed to the increased couple's sexual activity, unmasking the real cause of infertility or unexplained subfertility. Recently, some researchers investigated a sample of 50 couples with unexplained infertility, showing that 7 couples (14%) naturally conceived after several years (on average 2 ± 0.7 years) of infertility, precisely during the quarantine period (12). In our study, surprisingly, 4% of all infertile couples achieved a natural spontaneous pregnancy during the quarantine, despite the long duration of their infertility.

The response rate, calculated as the percentage

of people who joined the study, was quite low (18.2%). This data could be due to the psychological concerns related to infertility, as well as the perception of the physical distancing from professional health care assistance. In fact, it should be noted that, as a result of the rapid SARS-CoV-2 spread in Italy, ISS wisely recommended the suspension of treatments for couples who have not yet started pharmacological therapy. This probably has caused a long-term impact, leading a lot of couples to postpone the start of the ART program by a few months. The temporary closure of the ARTs clinics and services during the emergency period may have turned away the couples, increasing their fear of being neglected and impacting their desire for parenting.

In our study cohort, a small sample of couples decided to temporarily desist from their intention to conceive. The worries about potential viral effects on pregnancy and possibility of contagion in hospitals are the main reasons that led people to this conclusion. This could be explained by the fear and anxiety that media of communication created when they notified people about the pandemic. However, to date, the current available (21-23) data suggest that COVID-19 in pregnant women has a similar clinical presentation and illness severity to non-pregnant adults, without adverse maternal or perinatal outcomes.

Interestingly, only 13.3% of participants desisted from the plan due to the existence of conflicts, aggravated by the increased time spent together during COVID-19. A possible explanation of this small sample size could be that infertile couples had already been challenged by the imposed difficulties of an ART program. Therefore, they had already been transformed into couples who have a good resilience, based on their complicated and sad experiences in the past. The resilience of couples with a long history of infertility could be also related to their persistence, whereas couples with shorter duration of infertility decided more frequently to desist from their intention to conceive.

In our case series, the median patients' age was 39 years old. Our findings are consistent with data reported by the Italian National Institute of Statistics (ISTAT) with respect to the Italian general population, although our cases had specific history of infertility. In fact, currently, the mean age of first childbirth in our country is 32.4 years for women and 35.3 for men and Italy is ranked in the

second place among EU countries for delayed parenthood (13).

As referred by the participants, the type of planned ARTs was heterologous in 48.3% of cases. This data could be explained by the high implementation rate of oocyte/sperm donation programs in our area, Tuscany, as the first region in Italy to perform these treatments since 2014. The role of the psychologist is essential to support the couples in a productive counselling, helping them to scrutinize their situation in a constantly changing condition, reducing their self-blame feelings, and encouraging their assertiveness (24, 25). Regarding hospitalization, people knew they could not go to hospitals except for emergencies. These aspects open a debate on the possible subjective effects of the risk perception following the pandemic. Probably, the reason for termination of the plan to conceive was due to the worsened life expectancy of couples.

To the best of our knowledge, this is one of the first studies to investigate the potential changes that the COVID-19 period imposed on the desire for parenthood and the lifestyle of infertile couples waiting for ART programs. There are some recent studies in the literature that highlight how the prevalence of state-anxiety is high in women whose ART cycles were postponed due to COVID-19 according to literature findings regarding the prevalence of anxiety in infertile women. This specific study also highlights the effect of the outbreak on anxiety levels specifically in women whose ART cycles were delayed in this period (26). Other studies report that the psychological impact of COVID-19 pandemic on infertile couples who could have undergone IVF treatment is significant. The occurrence of these psychological symptoms was significantly associated with the time spent on COVID-19 related news per day, having partner with evidence of psychological disorder and, in females, with a diagnosis of poor ovarian reserve (27).

The greatest challenge in conducting this study was identifying validated questionnaires that represented specific aspects of parenting and sexuality during the pandemic. In fact, there are no specific validated questionnaires about the impact of the quarantine on reproductive purposes. In this regard, the research methodology was selected based on a previous scientific questionnaire designed to assess the impact of COVID-19-related control measures on couples' quality of life as

well as on their reproductive desire (6). This led to design a questionnaire that could be used to carry out future research on parenthood and infertility.

Conclusion

It seems that COVID-19 period negatively impacted the psycho-physical well-being of infertile couples, leading to considerably reduced scores of happiness, feeling energetic, and interest in life. Although most of these couples had prolonged infertility, a small number of cases achieved a spontaneous natural pregnancy during the lockdown, probably due to more couple intimacy and longer time spent together. However, major concerns about the consequences of the virus on pregnancy and the risk of contagion in the hospital have led a small number of infertile couples to decide to postpone their parenting project. This attitude may have created a further negative impact on couples' reduced desire for parenthood, which could result in a decline in births in the near future.

Conflict of Interest

None.

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