Comparison of spermiograms of men presenting due to infertility before and during the COVID-19 pandemic

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Abstract

Background: Following the rapid global spread of the novel coronavirus SARS-CoV-2, the World Health Organization declared COVID-19 a pandemic on March 11, 2020. Over the intervening year, there has been interest in the impact of both SARS-CoV-2 infection and pandemic-induced social restrictions on male reproductive health. This study aimed to evaluate the spermiogram values of men who presented to a urology clinic due to infertility during the pandemic and compare the results with those in the previous two years. Materials and Methods: Patients who presented to the urology outpatient clinic of Medical Park Antalya Hospital Complex for the first time due to infertility were included. The patients' age, semen volume, and spermiogram results were recorded. The patients were divided by presentation date into pre-pandemic group 1 (March 2018 - February 2019), pre-pandemic group 2 (March 2019 - February 2020), and the pandemic group (March 2020 - February 2021) for comparison. Results: A total of 594 patients were included in the study. There was no significant difference between the three groups in terms of the number of patients who presented (207, 190, and 197 patients, respectively; p=0.691). The mean age was 36.6±7.2 in pre-pandemic group 1, 35.5±7.1 in pre-pandemic group 2, and 33.1±6.3 in the pandemic group. Patients who presented during the pandemic were significantly younger (p<0.001). There was no difference in semen volume among the groups (p=0.910). Analysis of spermiogram results revealed no significant differences in normospermia and pathological spermiogram rates by year (p=0.222). Conclusion : In the first year of the COVID-19 pandemic, there was no significant difference in the number of men who presented for infertility or in their spermiogram results compared to 2018 and 2019. However, it is noteworthy that the patients were significantly younger during the pandemic than in the previous two years.

Introduction

The novel coronavirus disease (named COVID-19 by the World Health Organization [WHO]) spread from a cluster of unexplained pneumonia cases in Wuhan, China to a global public health emergency affecting every country in the world within months and was declared a pandemic by the WHO on March 11, 2020.[1] Throughout the intervening year, research has been ongoing to understand the health consequences of both SARS-CoV-2 infection and the new social order brought about by the pandemic. Before the COVID-19 pandemic, infertility was estimated to affect between 8% and 12% of couples of reproductive age worldwide, with male infertility known to be solely responsible for 20-30% of these cases and a contributing factor in 50% of all cases.[2] Since the start of the COVID-19 pandemic, several studies have been conducted on

the effect of the SARS-CoV-2 virus on the male reproductive system, especially testicular functions. These studies mostly focused on histopathological changes in testicular and semen parameters caused by COVID-19 infection, the presence of the virus in reproductive organs and semen, and its effect on sex hormones.[3–6] Despite the vaccination programs currently underway, concern that the pandemic will continue long term raises the question of what impact pandemic-imposed lifestyle changes will have on male reproductive health. The aim of this study was to investigate semen parameters in men presenting to the urology clinic due to infertility in the first year of the pandemic and to compare the results with those in the previous two years.

Materials and Methods

Men who presented to the urology outpatient clinic of the Medical Park Antalya Hospital Complex between March 2018 and February 2021 due to infertility were included in this study. Inclusion criteria were inability to achieve pregnancy for more than 12 months despite regular unprotected sexual intercourse[2] and presenting to our clinic with this complaint for the first time. Patients who presented for follow-up and those with previous infertility treatment were excluded from the study.

After a detailed history-taking and physical examination, semen samples obtained in sterile tubes by masturbation after an average of 3 to 5 days of sexual abstinence were analyzed after liquefaction at 37°C for 30 minutes. A Makler counting chamber was used to determine spermatozoa concentration and percentage of motile spermatozoa according to WHO 2010 criteria, and morphological evaluation was performed by light microscopy according to Kruger criteria after staining.[7] All semen samples were evaluated by the same specialist. Patient age, semen volume, and spermogram results were recorded. The patients were divided by presentation date into pre-pandemic group 1 (March 2018 - February 2019), pre-pandemic group 2 (March 2019 - February 2020), and the pandemic group (March 2020 - February 2021). The results were compared between these groups.

Ethical Considerations and Statistical Analysis

This retrospective study was approved by the Antalya Medical Park Hospital Complex Ethics Committee (approval no: 2021/03) and was carried out in accordance with the 1975 Helsinki Declaration. All statistical analyses were performed using SPSS statistical software (SPSS for Windows version 18.0; SPSS Inc, Chicago, IL, USA). Age and semen volume were expressed as mean ± standard deviation. The normality of the data distribution was assessed with Kolmogorov-Smirnov test. Age and semen volume were compared using Kruskal-Wallis test, and Mann-Whitney U test with Bonferroni correction was used for pairwise comparisons. Relative differences in the distribution of normospermia and pathological spermogram rates by year were compared with chi-square test. P values less than 0.05 were accepted as statistically significant.

Results

A total of 594 patients were included in the study. The number of patients who presented to the urology clinic for infertility did not differ significantly by year (in chronological order: 207, 190, and 197; p=0.691). The mean age was 36.6±7.2 in pre-pandemic group 1, 35.5±7.1 in pre-pandemic group 2, and 33.1±6.3 in the pandemic group. Patients who presented during the pandemic year were significantly younger ($p<0.001$). There was no difference in semen volume between the three groups (p=0.910). Analysis of spermiogram results revealed no significant differences in normospermia and pathological spermiogram rates by year (p=0.222). The spermiogram results of all three groups are shown in Table 1.

Discussion

To our knowledge, this study is the first in the literature to evaluate the effects of the COVID-19 pandemic on male fertility by comparing the demographic structure and spermiograms of patients presenting to a urology clinic due to infertility before and during the pandemic. The impact of the pandemic on semen parameters in men is a controversial issue, and may occur in two ways. The first is the effect of the infection itself, while the second involves the possible psychophysiological effects of pandemic-imposed social restrictions on male reproductive health.

In the pathophysiology of COVID-19 infection, host ACE2 receptors facilitate intracellular entry and replication of the SARS-CoV-2 virus. This process is much easier in cells with high ACE2 expression. In many studies, ACE2 expression level was found to be high in the seminiferous tubules and in Leydig and Sertoli cells. This potential affinity of the SARS-CoV-2 virus for the testicles is the main basis for the researchers who support this view. However, studies evaluating the effect of infection on semen parameters have yielded different results. In fact, it remains unclear whether the testicles and other male reproductive organs are susceptible to SARS-CoV-2 infection. Temiz et al. found that sperm quality decreased in the acute period of COVID-19 infection but did not differ from controls after treatment. They attributed the decrease in semen parameters during acute infection to high fever, but noted that SARS-CoV-2 was not detected by PCR in the semen during this period.[8] In another study, SARS-CoV-2 was detected by PCR in the respiratory tract but not testicular tissue in postmortem evaluations after COVID-related deaths.[9]

Levels of sex hormones in individuals infected with COVID-19 have also been investigated due to their direct effect on semen parameters. Male sex hormones vary dramatically with acute illness or physiological stress, so it should be kept in mind that these early results are may be disputable.[10] In a study of 119 patients, Ma et al. determined that luteinizing hormone and prolactin levels were higher in COVID-19 patients compared to the control group, but did not detect a significant difference in testosterone or estradiol levels.[5] In another study, pretreatment levels of follicle-stimulating hormone, leutinizing hormone, and testosterone levels were lower in 30 COVID-19 patients compared to the control group, while posttreatment levels did not differ significantly from those of controls.[8] In a study of 31 patients, Rastrelli et al. reported that testosterone levels were significantly lower in COVID-19 patients who required intensive care than in those with mild disease.[11] It seems that the conversation on the effect of COVID-19 infection on testicular functions cannot be closed yet.

Another important aspect of the COVID-19 pandemic is the major lifestyle changes that have occurred for many individuals. Social isolation due to the pandemic has led to increased feelings of loneliness as well as increased use of mobile devices and laptop computers. These devices may adversely affect semen parameters due to the low-level radio-frequency electromagnetic fields they produce.[12] In addition, obesity that can occur due to a sedentary lifestyle may also be an important risk factor. A meta-analysis study showed that semen quality was lower in obese men than in men of normal weight.[13]Psychosocial stress caused by the pandemic also constitutes a significant public health problem. The effect of psychosocial stress on semen parameters has actually been a topic of debate for a long time. Hjollund et al. determined in a prospective study that there was no relationship between stress and sperm parameters[14], whereas Janevic et al. found a negative association between stress and sperm concentration, motility, and morphology.[15] As the duration and degree of stress experienced by a lonely man cannot be measured with objective parameters, the effect of stress on semen parameters remains uncertain. The results of the present study suggest that these pandemic-related risk factors are not severe enough to disrupt sperm parameters. Of course, these one-year results can also be seen as a preliminary study. If the pandemic continues, future studies of larger series will offer more insight into this issue.

It is also necessary to question the sex life of patients who present due to male infertility during the COVID-19 pandemic. Analyzing semen parameters alone may not be enough in these patients. It has been seen in pandemics that patients affected by mental disorders far outnumber the infected patients.[16] Therefore, it should be kept in mind that increased anxiety or depression in men during the pandemic can also cause erectile dysfunction (ED) and loss of libido.[17] An individual's psychological state may trigger or exacerbate ED. Depression has been found to double the risk of ED.[18] ED may in turn cause a loss of self-esteem, which can adversely affect their partner relationship. Therefore, performing a psychological evaluation is recommended before seeking an organic cause for ED, especially in men under the age of 40.[19]

Another issue that may be important during the pandemic is loss of libido.[20] Although this condition (also known as hypoactive sexual desire disorder) is less common in men than women, it can lead to important problems between couples.[21] In a prevalence study by Carvalheria et al., loss of libido lasting more than 2 months was most commonly seen among men aged 30 to 39 years.[22] Clinicians should bear in mind that low

libido is not only caused by low testosterone levels, but can also occur as a side effect of antidepressant and antipsychotic drugs.[23] Furthermore, sexual performance anxiety, relationship problems between couples, and depression/anxiety are known to reduce sexual desire.[24]

One of the important findings of our study was that the mean age of men presenting due to infertility during the pandemic was 33.1±6.3 years, significantly younger than in the previous two years. This difference may reflect an increase in future anxiety in these patients during the first year of the pandemic. A study in the literature demonstrated that the prevalence of anxiety/depression during the COVID-19 pandemic increased significantly more among participants under 35 years of age than in participants over 35 years of age.[10] According to the definition of infertility, pregnancy is not achieved for 12 months despite timed or regular sexual intercourse. Therefore, a detailed history should be obtained from infertile couples to understand the frequency of sexual intercourse during the COVID-19 pandemic. The lack of difference in the number of patients presenting to the clinic due to infertility compared to the previous two years indicates that there was no change in couples' desire to have children, despite the adverse circumstances brought about by the COVID-19 pandemic.

In summary, the available data suggest that for patients who present due to infertility during the pandemic and have no major problems with semen parameters, a thorough history should be obtained, as well as psychiatric evaluation to question sex drive and presence of ED.

In this study, the lack of data regarding whether the patients who presented during the pandemic had a history of COVID-19 infection may be seen as a limitation. However, the main objective of this study was not to evaluate the effect of COVID-19 infection specifically, but demonstrate the overall impact of the pandemic. Therefore, this study did not examine history of COVID-19 infection in the patients who presented during the pandemic year.

Conclusion

During the first year of the COVID-19 pandemic, there was no significant difference in the number of men who presented to the urology outpatient clinic due to infertility or their spermiogram results when compared with data from 2018 and 2019. However, the men who presented during the pandemic were significantly younger than those in the previous two years. Questioning psychosexual behavior may also be considered when evaluating infertile men during the pandemic.

Authors contribution:

MS project development and manuscript writing and editing, MD project development, Manuscript writing and editing, ME data analysis, SSU data analyasis, AS data collection, EK data collection, HT manuscript writing and editing

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`Table 1 Spermiogram results by year.docx` available at https://authorea.com/users/734988/articles/711629-comparison-of-spermiograms-of-men-presenting-due-to-infertility-before-and-during-the-covid-19-pandemic