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The Effect of SARS-Cov2 Infection on The Spermogram: A Prospective Study

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Abstract

Background: During the Coronavirus disease 2019 (COVID-19) pandemic, there was always concern about damage to different organs of the body. In this study, we aimed to determine if coronavirus 2 (SARS-CoV-2) could influence the sperm parameters in inpatient adult men with COVID-19.

Materials and Methods: In this prospective study during 2021, 22 patients with COVID-19 diagnosed with polymerase chain reaction (PCR) test and clinical symptoms and history of admission and 19 volunteer healthy men as the control group participated. They were asked to provide semen samples at 2 and 6 months after hospital discharge and the same time for the control group. The following parameters were measured in all semen samples and beside the demographic data, they compared between the two groups: volume (mL), sperm concentration (10^6/mL), total motile sperm percentage, progressive percentage, normal morphology percentage, and DNA fragmentation index (DFI).

Results: The mean ± SD age of the participants in the COVID and control groups was 46.36 ± 9.94 and 45.84 ± 10.21 years, respectively (P=0.869). The mean ± SD body mass index (BMIs) of the participants in the COVID and control groups were 28.6 ± 5.460 and 29.6 ± 6.092, respectively (P=0.579). The mean ± SD number of children was 1.41 ± 1.054 in the COVID group and 1.47 ± 1.073 in the control group (P=0.847). All the sperm parameters were significantly impaired after 2 months in the COVID group in comparison with the control group (P<0.05). After 4 months from first sampling, all the parameters were improved significantly (except normal morphology) but had not yet reached the level of the control group.

Conclusion: SARS-CoV-2 affected semen parameters in patients admitted because of COVID-19, in the short term. It is expected that this will improve with time.

Keywords: Coronavirus SARS, Male Infertility, Semen Quality Analyses, Spermatogenesis

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Introduction

Coronavirus 2 (SARS-CoV2), as a severe acute respiratory syndrome, has infected millions of people since December 2019 that first reported from Wuhan, China (1). The Coronavirus disease 2019 (COVID-19) affects different body organs including the respiratory system, liver, kidney, heart, the gastrointestinal, hematological and nervous systems with a high rate of multi-organ failure and mortality (2).

Although, there are limited studies about andrological consequences of COVID-19, there is no consensus about its effect on semen quality (3, 4). Whether COVID-19 is detectable in semen fluid or not is debatable. In the evaluation of male patients with COVID-19 and those recovering from the disease, Li et al. (5) identified SARS-CoV-2 in semen fluid. In contrast, there are some other studies that do not confirm this finding (6, 7). COVID-19 may affect the testis parenchyma, changes the Sertoli

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and Leydig cells morphology, and causes lymphocytic inflammation (8). It may have a negative impact on semen quality and sex hormones, although it may be reversible (9- 12). There are limited studies about COVID-19 effects on the semen quality, therefore we designed the present study.

Material and Methods

The institutional board of research and Ethics Committee of Shahid Beheshti University of Medical Sciences confirmed the study protocol (IR.SBMU.RETECH.REC.1399.559). This study was conducted in accordance with the Declaration of Helsinki. All participants signed the informed consent.

Participants

Patients participating in this study were 20-60 years old male volunteers who had been diagnosed COVID-19 infection based on a nasopharyngeal SARS-CoV-2 real-time (RT) polymerase chain reaction (PCR) swab during their admission to Shohada-e-Tajrish or Taleghani Hospitals. They were divided into mild, moderate or severe groups depending on clinical characteristics and radiological findings (13, 14). Semen samples were collected from them at 2 and 6 months after hospital discharge. All patients were treated with the specified protocol (15). Their demographic data and the COVID-19 disease history were recorded.

In parallel, the semen fluid of 19 volunteered men which was obtained by masturbation was evaluated as the control group, at the beginning of the project. The control group was the men who live a normal life in society without any symptoms of COVID 19. They did not present any suspicious symptoms, including constitutional symptoms, fever, cough, gastrointestinal symptoms or any other symptoms that made us suspected of having COVID 19. All semen samples were collected by masturbation following sexual abstinence of 1-3 days. All semen analysis was evaluated according to WHO 2010 criteria (16) at the Andrology Laboratory of In Vitro Fertilization Center, Taleghani Hospital, Tehran, Iran. Participants who could not provide the second semen sample were excluded. Also, participants with orchitis or abnormal findings on scrotal examination including severe varicocele, history of vasectomy, testis torsion, single testis, testis trauma and any kind of scrotal -inguinal surgery were also excluded. All the participant characteristics including body mass index (BMI), age, history of smoking and the number of children were recorded.

Andrology assessment

The following parameters were measured in all semen samples (16) and compared between the two groups: volume (mL), sperm concentration (10^6/mL), total motile sperm, progressive percentage, normal morphology percentage (assessed by Strict criteria) and DNA fragmentation index (DFI, assessed by sperm chromatin dispersion). Sperm motility is the movement, or swimming of sperms. The progressive sperm motility defined as sperms that move along a straight line or around large circles which is necessary for pregnancy (17).

Statistical analysis

Quantitative data with normal distribution are shown as a mean ± standard deviation. To compare proportions and means, we used chi-square and Student's t tests, respectively. $P<0.05$ was considered statistically significant. SPSS software version 26 (IBM Corporation, Armonk, NY, USA) was used for statistical analysis.

Results

Totally, 41 men (22 patients with COVID-19 and 19 volunteers as the control group) participated in this study. Table 1 shows the demographic data of our groups.

Table 1: Participant's demographic characteristics

Characteristics	COVID group (n=22)	Control group (n=19)	P value
Age (Y)	46.36 ± 9.94	45.84 ± 10.21	0.869
Number of children	1.41 ± 1.054	1.47 ± 1.073	0.847
Smoking	11 (50)	11 (57.9)	0.756
BMI (kg/m^2)	28.6 ± 5.460	29.6 ± 6.092	0.579
COVID19 severity			
Mild	12		
Moderate	10		
Severe	0		

Data are presented as mean ±SD or n (%).

The sperm parameters including sperm motility, sperm concentration, progressive sperm percentage, normal morphology, and DFI were determined in each group and compared (Table 2). Six months after discharge, since the control group did not refer, we compared the patients' semen parameters to the baseline semen parameters of the same group through the paired t test. We also compared the second sperm analysis with the COVID-19 group after six months to the baseline sperm analysis of the control group that the results are shown in Table 2. As shown in Table 2, all the sperm parameters were impaired significantly in the COVID group at month two, in comparison with the control group. After a 6 months follow-up from discharge, all the parameters (sperm concentration: $P=0.005$, sperm motility: $P<0.001$, progressive sperm: $P=0.045$, DNA fragmentation index: $P=0.001$) were improved significantly except normal morphology ($P=0.066$), in the COVID group in comparison with themselves in the time points, 0 and 2 months after COVID-19 affection but it had not yet reached the level of the control group.

Table 2: Comparison sperm parameters between the COVID and control groups at 2 and 6 months

Sperm parameters	COVID group baseline	Control group	P value*
Sperm concentration (million/ml)	29.09 ± 14.46	63.74 ± 21.16	<0.001
Sperm motility	32.27 ± 11.61	60.05 ± 10.71	<0.001
Progressive motility	16.86 ± 10.27	46.32 ± 14.22	<0.001
Normal sperm morphology	0.66 ± 0.83	2.42 ± 1.21	<0.001
DNA fragmentation index	39.8 ± 15.28	14.4 ± 4.78	<0.001
	COVID group baseline	**COVID group after 6 months**	**P value****
Sperm concentration (million/ml)	29.09 ± 14.46	39.14 ± 16.84	0.005
Sperm motility	32.27 ± 11.61	49.05 ± 16.50	<0.001
Progressive sperm	16.86 ± 10.27	31.23 ± 14.12	0.045
Normal sperm morphology	0.66 ± 0.83	1.05 ± 0.95	0.066
DNA fragmentation index	39.8 ± 15.28	27.91 ± 12.35	0.001
	Control group	**COVID group after 6 months**	**P value***
Sperm concentration (million/ml)	63.74 ± 21.16	39.14 ± 16.84	<0.001
Sperm motility	60.05 ± 10.71	49.05 ± 16.50	0.015
progressive sperm	46.32 ± 14.22	31.23 ± 14.12	0.002
normal sperm morphology	2.42 ± 1.21	1.05 ± 0.95	<0.001
DNA fragmentation index	14.4 ± 4.78	27.91 ± 12.35	<0.001

Data are presented as mean± SD. *; Independent sample t test and **; Paired t test.

Discussion

The COVID19 and consequent severe acute respiratory syndrome has the ability to attack multiple organs and weaken overall immunity for months (18, 19). The man's fertility system may be affected by various infectious or viruses including mumps virus, influenza virus, human immunodeficiency virus (HIV), Zika virus and may even involve the testes tissues (16).

Pneumonia is the most common clinical manifestation of COVID-19, due to the presence of Angiotensin-converting enzyme 2 (ACE2)-containing cells among type 2 alveolar cells (20). The expression level of ACE2 in the Sertoli and Leydig cells, may be even higher than the alveolar type II cells. Testicles with ACE2 receptor may be vulnerable to the COVID-19 infection, which may become a target organ such as lungs (21).

A review study of evaluating biological implications of the COVID-19 on sexual transmissibility, fertility and viral presence, revealed that COVID-19 is potentially present in seminal fluid, but sexual transmission not reported (22). Previous epidemiologic studies show significant concerns regarding the long-term fertility capacity for patients who are their reproductive system affected by the Sars-CoV-2 (23). A systematic review for survey the potential impact of COVID-19 on male reproductive organs and male fertility concluded that, only one of the 28 studies had reported the presence of SARS-CoV-2 in the seminal fluid (24). They observed a decrease in semen quality in the patients with moderate infection rather than patients with mild infection and healthy controls. Impairment quality of seminal fluid may be related to inflammation and fever occurrence (5).

In our study, the seminal fluid analyses of the admitted patients with COVID-19 were compared between the period of disease and at least six months after discharge of hospital from COVID-19 and control groups. The long-term effect of COVID-19 on male fertility is a debate. A systematic review study compared parameters of seminal fluid in patients recovered from COVID-19 revealed seminal fluid volume, progressive sperm motility and sperm concentration were not significantly decreased after getting the disease. Mean sperm count and total sperm motility between the COVID-19 group and control group were statistically significant (25). Guo and colleagues found that the total sperm count, sperm concentration and progressive motility following recovery from the COVID-19 infection increased significantly after 84 days in comparison with the first 56 days of recovery (9). In another study, COVID-19 affected sperm parameters, as well (26). A prospective study of men who were recovered from the COVID-19 infection revealed that 25% of them were oligocrypto-azoospermic. From eleven men with seminal fluid impairment, eight were azoospermic and three were oligospermic. Thirty three patients (76.7%) showed pathological levels of IL-8 in seminal fluid. Oligo-crypto-azoospermia was significantly correlated with COVID-19 severity (27). All these studies approve our results about the effect of COVID19 on sperm quality.

Every febrile disease could lead to impaired semen quality and even azoospermia (28). Due to the nature of the spermatogenesis cycle, we evaluated the samples

two months and 6 months after hospital discharge in the COVID group to prevent the effect of febrile disease on sperm quality.

The studies that mentioned above and the present study showed that seminal fluid parameters and male fertility may be affected by COVID-19. The possibility of this fact that COVID-19 infection would affect the sexual function and male reproductive system and permanent effects on the human reproductive health should be evaluated long-term, multicenter, and prospective cohort studies with larger sample sizes. Here, we evaluated patients with a COVID-19 infection who needed to be hospitalized unlike most studies that considered outpatients. It seems that hospitalized patients experience severe degrees of illness than outpatients, what made our study differ of other published studies. Although, our present study is not free of some limitations, including low sample size, analyze other parameters such as sperm leukocyte count, sex hormones, anti-sperm antibodies which could provide useful information and long term follow up. Also, the follow-up semen analysis of the control group was impossible for us.

Conclusion

In this study, we concluded that SARS-CoV-2 affects semen parameters in patients who were admitted to the hospital because of COVID-19, in the short term. After the disease recovery, these parameters start to improve, but studies with larger sample size and longer follow up time are necessary to prove whether the parameters return to their previous level or not.

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Authors' Contributions

F.A., M.K., M.A., S.S., B.N., A.F., M.D.; Participated in study design and data collection. F.A., B.N., M.D.; Participated in statistical analysis and drafting. All authors read and approved the final manuscript.

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