COVID-19-induced seminal alterations in Qalyubbia Governorate, Egypt

Original Article

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ABSTRACT

Background: A variety of viruses, including influenza and mumps virus can disrupt male reproductive function and potentially infect the testes. The pandemic COVID-19 has the ability to damage multiple organ systems. The male genitalia could be one of its targets.

Aim: The purpose of this study was to determine how COVID-19 affected sperm characteristics.

Patients and Methods: A cross-sectional case control study with 100 fathers who had recovered from COVID-19 three months before starting the study and 100 fathers of similar age who were healthy served as controls. Semen of all participants was analyzed utilizing computer-assisted semen analysis.

Results: Patients who had recovered from COVID 19 had significantly lower sperm parameters than controls including sperm concentration, progressive and total motility (P<0.001). There was no correlation between sperm count, motility, morphology index, or teratozoospermia with illness severity. Abnormal semen analysis could be predicted from the duration of COVID-19 infection..

Conclusion: COVID-19 negatively impacts the male reproductive system, at least temporarily.

Key Words: Coronavirus disease 2019 (COVID-19), semen, sperm, testis.

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INTRODUCTION

A variety of viruses, including influenza and mumps virus can disrupt male reproductive function and potentially infect the testes[1]. Feverish conditions can have a negative impact on testicular functions[2].

Due to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a new global viral outbreak known as coronavirus disease 2019 (COVID-19) has emerged (SARS-CoV-2)[3]. Men have more severe disease and a higher fatality rate than women[4,5]. It primarily causes respiratory dysfunction, but other systems may be impacted. COVID-19 patients have viral particles found in numerous organs[6].

Transmembrane serine protease 2 enzyme as well as angiotensin-converting enzyme 2 receptor are required for SARS-COV-2 cell invasion and proliferation[7]. Leydig cells and the seminiferous duct of the testis both exhibit significant expression of angiotensin-converting enzyme 2, whereas seminal vesicles and glandular cells exhibit weak expression. Additionally, the prostate, epididymis, and seminal vesicle have all been found to express transmembrane serine protease 2[8,9].

The relationship between SARS-CoV-2 and male genital organs is a subject of substantial debate. Numerous questions were investigated by researchers. First, check to see if the semen contains any virus particles. Second, may COVID-19 impact testicular functions and if so, how? As a result, we wanted to investigate how semen qualities varied generally between those recovered from COVID-19 and those who were not infected.

PATIENTS AND METHODS

Patients

This cross-sectional case–control study was undertaken at the Benha Faculty of Medicine's Andrology outpatient clinic from January 2022 to October 2022. Two age-matched groups of fathers were included in the study. Group 1 comprised of 100 fathers who had recovered from COVID-19 3 months prior to participating in the study (confirmed PCR-negative), and group 2 consisted of 100 fathers who had not been infected with COVID-19 in the previous 3 months as a control group. Patients who had sexual dysfunctions prior to COVID-19, were single,

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had an acute infection, had a history of varicocele, or had problems of reproduction were eliminated.

Methods

All patients were provided a thorough medical history and underwent a clinical examination with particular attention paid to the genitalia. Patients who had recovered from COVID-19 were questioned regarding their past experiences with infection-related symptoms such fever, coughing, sore throat, and the necessity for and type of required hospital stay. According to China's National Health Commission's New Coronavirus Pneumonia Prevention and Control Program, the disease severity was determined[10].

Semen collection

Semen samples were collected from all the participants via masturbation in accordance with the WHO laboratory guidelines[11] and analyzed using Computer-Assisted semen Analysis.

Ethical considerations

The Benha Faculty of Medicine's ethical committee on research involving humans approved the study's protocol (MS 16-9-2021) after it had been approved by the Department of Dermatology, Venereology, and Andrology. Before taking part in the study, each individual gave their informed, written, and signed consent.

Statistical analysis

The statistical software for social science (SPSS), version 26 (IBM SPSS, IBM Corp., Armonk, New York, USA) was used to examine the data. Mean, SD, number, and percent descriptive statistics were produced for the data. Analytical statistics: the Mann–Whitney *U*test (*z*) was used for intergroup analysis for continuous nonparametric data, and the Student's *t*test was used to compare the means of two groups of numerical (parametric) data. Analysis of variance was used to compare numerical (parametric) data between more than two groups. The Kruskal–Wallis test (*z*) was employed for intergroup analysis on continuous nonparametric data. Using the χ^2test, categorical data were compared between groups (χ^2value). Different parameters were correlated using a Pearson correlation coefficient (*r*) test. A logistic regression model was used to determine which of the analyzed parameters were significant predictors. Statistics were judged significant at *P* value less than 0.05 (S).

RESULTS

The demographic and clinical characteristics of COVID-19 recovered men who took part in this study were reported, with a mean age of 33.50±6.49 years compared with controls (35.13±9.17 years). Illness duration (15.54±4.683) ranged from 7 to 30 days in 91/100 (91%), cough in 80/100 (80%), shortness of breath in 82/100 (82%), hospitalization in 14/100 (14%), seven cases admitted to ward, seven cases admitted to ICU, and 9/100(9%) patients did not receive drugs.

When compared with controls, the patient group had statistically significant lower sperm parameters (concentration, total count, progressive motility, total motility, and morphological index) but remained within normal ranges (Table 1).

Table 1: Comparison between study groups regarding semen analysis parameters

	Group 1(N=100)	Group 2 (N=100)	Test of significance	*P* value
	Mean±SD	Mean±SD		
Volume	3.47±1.63	2.91±0.72	*t*=3.1	0.002*
Liquefaction time	34.65±18.75	34.80±0.98	*t*=0.1	0.9
Concentration	49.97±32.77	87.21±29.78	*z*=8.4	<0.001*
Total sperm count	159.06±124.39	254.60±122.55	*z*=5.5	<0.001*
Progressive motility	39.36±17.49	52.80±11.37	*t*=6.4	<0.001*
Rapid progressive	17.76±12.66	23.22±9.20	*t*=3.5	<0.001*
Slow progressive	21.68±9.06	29.85±7.39	*t*=6.9	<0.001*
Total motility	48.77±19.53	72.86±8.90	*t*=11.2	<0.001*
Morphology index	27.55±8.25	32.08±12.56	*t*=3.1	0.001*
Teratozoospermia sperms	72.50±8.29	67.91±12.57	*t*=3.1	0.001*

* Significant

Group 1 had a considerably higher volume of semen than group 2. The mean was 3.47±1.63ml in group 1 and 2.91±0.72ml in group 2 (*P*=0.002). With no significant difference, the mean liquefaction time in group 1 was 34.65±18.75s compared with 34.80±0.98s in group 2. Teratozoospermia was substantially higher in group 1 than in group 2. The mean in group 1 was 72.50±8.29 against 67.91±12.57 in group 2 (*P*=0.001). Based on the COVID-19 classification of severity by history of manifestations, it was shown that age has a statistically significant impact

on severity (P=0.02, Table 2). Semen features did not, however, significantly change between mild, moderate, and severe instances (Table 3). A statistically significant inverse correlation between sperm parameters and the length of the COVID-19 sickness was discovered. The relationship between sickness duration and liquefaction time was not statistically meaningful (r=0.013, P=0.902) (Table 4). In univariate analysis, the presence of COVID infection and a longer duration of illness were significant predictors of abnormal semen results (Table 5).

Table 2: Correlations between severity of infection and different parameters

	Severity of infection	
	r	*P* value
Age	0.256	0.010*
Duration of marriage	0.093	0.356
Volume	0.030	0.768
Liquefaction time	0.074	0.464
Concentration	-0.084	0.406
Total sperm count	-0.065	0.523
Progressive motility	-0.064	0.526
Rapid progressive	-0.057	0.573
Slow progressive	-0.047	0.645
Total motility	-0.078	0.440
Morphology index	-0.069	0.498
Teratozoospermia sperms	0.068	0.501

* Significant

Table 3: Comparison of semen analysis parameters regarding disease severity

	Mild (N=16)	Moderate (N=33)	Severe (n=51)	Test of significance	*P* value
	Mean±SD	Mean±SD	Mean±SD		
Volume	3.37±1.35	3.46±1.53	3.51±1.79	*f*=0.1	0.9
Liquefaction time	35.94±22.89	30.30±3.29	37.06±22.65	*z*=1.4	0.3
Concentration	51.86±24.20	54.29±34.49	46.59±34.11	*z*=0.6	0.6
Total sperm count	169.33±110.84	167.04±123.25	150.68±130.69	*z*=0.2	0.8
Progressive motility	43.75±13.90	37.61±18.20	39.12±18.09	*f*=0.7	0.5
Rapid progressive	21.16±12.53	16.09±12.85	17.79±12.61	*f*=0.9	0.4
Slow progressive	22.58±6.46	21.74±7.99	21.35±10.42	*f*=0.1	0.9
Total motility	52.25±14.23	48.80±19.31	47.66±21.23	*f*=0.3	0.7
Morphology index	35.78±13.65	30.42±13.30	32.00±11.71	*f*=0.9	0.4
Teratozoospermia sperms	64.22±13.68	69.58±13.30	67.99±11.71	*f*=0.9	0.4

Table 4: Correlations between duration of illness and different semen parameters

	r	*P* value
Volume	-0.228	0.023*
Liquefaction time	0.013	0.902
Concentration	-0.209	0.037*
Total sperm count	-0.300	0.002*
Progressive motility	-0.274	0.006*
Rapid progressive	-0.361	<0.001*
Slow progressive	-0.346	<0.001*
Total motility	-0.240	0.016*
Morphology index	-0.257	0.010*
Teratozoospermia sperms	0.292	0.003*

* Significant

Table 5: Logistic regression analysis of various variables for prediction of abnormal semen finding

	Univariate analysis			
	P values	OR	95%CI	
Age (years)	0.442	1.018	0.973	1.064
COVID-19 infection	<0.001*	7.027	2.581	19.137
Severity of infection	0.096	1.758	0.904	3.417
Duration of illness	0.012*	1.131	1.027	1.245

CI, confidence interval; COVID-19, coronavirus disease 2019; OR, odds ratio.
* Significant

DISCUSSION

Conflicting results have been found about the presence of SARS-CoV-2 in semen. While Li *et al.*[4] discovered SARS-CoV-2 RNA in the ejaculated semen; numerous other researches did not[12–17]. Spermatogenesis is a complicated biological process. A primordial germ cell takes an average of 74 days to grow into a mature sperm[18]. To analyze the possible impact of COVID-19 on male fertility, we compared the overall semen parameters of COVID-19 patients 3 months after recovery to those without COVID-19 infection.

In comparison to controls, COVID-19 recovered patients had significantly lower sperm concentration, sperm motility, and morphological index values. Additionally, the COVID-19 group experienced a statistically significant increase in teratozoospermia in line with other researches[19–22].

In line with the current findings, it was observed that patients recovering from moderate infection (25.5 days on average) had a substantial drop in sperm concentration, total number of sperm, and total number of progressive motility when compared with the control group[12]. Similarly, examined sperm samples of 12 patients 56–109 days after COVID-19 diagnosis showed reduced sperm motility[17]. Nevertheless, no significant differences were found between before and after COVID-19, except for a lower morphological index[23]. Longitudinal studies revealed a steady improvement in sperm measures after COVID-19 recovery[19,24].

The severity of COVID-19 infection did not have a significant impact in modifying semen parameters among patients of the current research. In contrast to other studies who found statistically significant differences between mild and moderate symptomatic groups[12,20]. SARS-CoV-2 RNA was discovered in urine and semen, as well as serious illness was linked to azoospermia[25].

Contrarily, no significant variations in semen parameters before and after SARS-CoV-2 infection were found at least 3 months following COVID-19 diagnosis, with the exception of a decrease in total motility[26]. In virally infected males, a number of factors, such as fever, the virus itself, medications, disinfectants, and even psychiatric issues, might affect the quality of their ejaculates[27]. Orchitis or epididymo-orchitis is thought to develop in 10–22% of men with acute COVID-19 infection, perhaps as a result of a testicular infection[12,16,28,29]. This was not the case in the study since we eliminated guys who were actively infected.

SARS-CoV-2 may harm the male reproductive system due to fever[30]. It has been proven that fever-induced increases in intratesticular temperature influence sperm parameters, and that it takes 3 months to return to baseline values[31]. In the investigation, however, semen measurements did not normalize after 3 months. On the contrary, the idea that COVID-19 fever had a negative impact on semen parameters was rejected[20].

The presence of coronavirus receptors in testicular cells suggests that the virus could enter and disrupt spermatogenesis[5]. In testicular autopsies of patients who died as a result of COVID-19, elevated apoptotic cell concentrations in testicles and epididymis were found, suggesting an autoimmune orchitis, and RT-PCR found the virus in 17% of samples[32–34]. Nonetheless, it was stated that it is likely that the samples were contaminated with blood rather than testicular tissue[32].

Immune cells like macrophages and virus-specific T cells may be recruited by SARS-CoV-2 entry into the testis, which may increase inflammatory alterations in the testis but may also promote virus clearance[16]. The inflammatory state may disrupt the blood–testis barrier. Nevertheless, in COVID-19 men, orchitis is not a common complaint[10].

Possible explanations for the findings include, first and foremost, the mental stress displayed by the majority of the patients. A negative relationship between emotional stress and spermatogenesis was observed[35–37]. Second, 91/100 (91%) of the patients in the current study had fever, and previous studies have found that patients with febrile sickness have temporarily lower semen parameter values[2,31]. Third, the unfavorable effects of COVID-19 medications[12], where it was discovered to reduce sperm characteristics in hospitalized patients but not in patients receiving home care.The disparity between the findings and those of other research could be explained by differences in

age groups, the composition of control groups, the level of medical care and therapies.

However, the findings of the majority of published publications on COVID-19's impact on male fertility should be viewed with caution due to the lack of pre-COVID-19 sperm parameters. Another disadvantage of earlier studies analyzing semen of patients before and after COVID-19 is the difficulty and illogical thinking of taking a specimen from a normal person, waiting until he contracts the condition, and then asking him to take another semen sample. As a result, we structured the work by selecting dads (a sure marker of fertility) who had babies within 1 year of enrolling in the study, and this can be considered a source of strength.

Limitations of the present study are the small number and absence of long-term follow up and repeated semen analyses. Accordingly the study makes flash on short-term effects of COVID-19 on sperm quality.

Based on the evidence presented above, COVID-19 infection definitely affects male reproductive systems by changing all semen characteristics without a defined mechanism. Clinicians should pay closer attention to the genitals as well as the lung and cardiovascular systems. Long-term and multicenter research should be conducted.

CONFLICT OF INTEREST

There are no conflicts of interest.

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