Adverse sexual effects of COVID-19 in a sample of Egyptian male patients

Original Article

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ABSTRACT

Background: COVID-19 is a pandemic caused by the SARS-CoV-2 virus, which causes severe acute respiratory syndrome. By the end of November 2022, numbers issued by the WHO indicate that over 600 million persons were infected by the disease and more than 6 million deaths occurred due to it.

Aim: The purpose of this study was to evaluate sexual functions in freshly recovered COVID-19 male patients.

Patients and Methods: A case-control study was undertaken on two groups of age-matched males: Group 1: 120 men one month after recovering from COVID-19 infection, and Group 2: 120 normal men as a control group. All subjects underwent a thorough clinical examination and full history taking. The 15-item International Index of Erectile Function (IIEF-15) was used to assess sexual functions. Total testosterone and prolactin levels in the blood were evaluated..

Results: Cases compared with controls exhibited significantly greater prolactin (19.9±13.9, 7.7±4.4, respectively, $P < 0.001$) and much lower testosterone levels (3.91 ± 2.31, 5.04 ± 2.22, respectively, $P < 0.001$), and their mean erectile function (EF) was significantly lower(22.5±3.7, 25.8±2.7, respectively, $P < 0.001$). EF 14-25 was present in the majority of the cases (n=83, 69.2%), with only two cases having EF less than 14. When compared to the control group, cases had significantly reduced mean orgasmic function, sexual desire, intercourse satisfaction, total sexual satisfaction, and overall IEF.

Conclusion: COVID-19 infection has a negative impact on male sexual functions.

Key Words: Coronavirus disease 2019, prolactin, sexual functions, testosterone.

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a pandemic brought on by the SARS-CoV-2 virus, which causes severe acute respiratory syndrome. Droplet infection is the main mode of transmission for SARS-CoV-2. Acute respiratory distress syndrome, pneumonia, and multiorgan dysfunction, including dysfunction of the male genitalia, may develop as a result[1].

It appears that a high body temperature brought on by a long-lasting fever may cause a subsequent autoimmune reaction that results in an autoimmune orchitis. Additionally, the SARS-CoV-2 virus enters cells through the angiotensin-converting enzyme 2 (ACE2), and the male genital system exhibits high levels of ACE2 expression[2]. All of these early results imply that COVID-19 may have an effect on men's reproductive health long after they have recovered.

Most articles in the literature focus on the sexual effects of COVID-19 during an active infection rather than after recovery. Sexual diseases are complex illnesses with both organic and psychological causes. The precise processes that could account for the correlation between COVID-19 and male sex are yet lacking. The purpose of this study was to assess sexual functions in freshly recovered COVID-19-infected men.

PATIENTS AND METHODS

Participants

This cross-sectional, case-control study was conducted from July 2021 to August 2022 in the Andrology outpatient clinic, Benha Faculty of Medicine. Two age-matched groups of males participated in this investigation. Group 1 consisted of 120 men who had recovered from COVID-19 infection1 month before, and group 2 was a control group of 120 men who were healthy.

Inclusion criteria

The following were the inclusion criteria:

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(1) Married men who had recovered from COVID-19 infection 1 month before study enrollment.

(2) They were sexually active before contracting COVID-19.

Exclusion criteria

The following were the exclusion criteria:

(1) Patients having chronic conditions such as hypertension and diabetes.

(2) Men suffering from acute infection with COVID-19.

(3) History of sexual disturbances.

(4) Those who have already received treatment for anxiety or depression.

All participants underwent a thorough history taking, clinical examination, and sexual function evaluation. The 15-item International Index of Erectile Function (IIEF-15) was used to evaluate the presence of sexual dysfunction[3]. To facilitate engagement with participants, a validated Arabic version was deployed. In addition, serum concentrations of total testosterone (tT) and prolactin (PRL) were measured.

Ethics Statement

This study was authorized by the Dermatology, Venereology, and Andrology department, and then by the Benha Faculty of Medicine's ethical committee on research involving human beings (MS.8-7-2021). Furthermore, all subjects provided informed written signed consent before participating in the study.

RESULTS

The current study included 120 individuals who had recovered from COVID-19 infection 1 month before enrolling in the study. Their age ranged from 24 to 52 years, with a mean age of 39.7 years. Cases came from a variety of locations, with 59.2% of them being urban and 40.8% being rural. There was no significant difference between cases and controls in terms of residence or educational level, with the majority of them (78.3%) having a university education, followed by 17.5% with a secondary education and 4.2% with a primary educational level. In comparison with the control group, cases had significantly greater PRL and lower tT (median=15.8 vs. 6.4, P =0.001; median=2.4 vs. 6.9, P =0.001, respectively) (Table 1). There were no statistically significant correlations between PRL or tT and clinical data of studied patients (Tables 2, 3).

Although EF less than 14 was observed in two cases but not in the control group, EF more than or equal to 25 (79.2%) was present in the majority of controls and in 29.2% of cases. The mean EF in patients was significantly lower than in controls (mean=22.5 vs. 25.8, P =0.001) (Table 1).

Table 1: Comparison of the data between the studied groups

	Control (N=120)	Cases (N=120)	*P* value
Age (years)			
Mean ±SD	37.5±6.5	39.7±7.9	0.261
Range	25–49	24–52	
Residence [n (%)]			
Rural	59 (49.2)	49 (40.8)	0.194
Urban	61 (50.8)	71 (59.2)	
Level of education [n (%)]			
Primary	5 (4.2)	5 (4.2)	0.131
Secondary	34 (28.3)	21 (17.5)	
University	81 (67.5)	94 (78.3)	
Prolactin (ng/ml)			
Mean ±SD	7.7±4.4	19.9±13.9	<0.001
Median	6.4	15.8	
Range	2.10–15.94	4.89–93.62	
Testosterone (ng/ml)			
Mean ±SD	6.6±1.8	2.6±1.1	<0.001
Median	6.9	2.4	
Range	2.34–9.30	1.32–5.72	

Erectile function of IIEF			
Mean ±SD	25.8±2.7	22.5±3.7	<0.001
Range	19–30	10–30	
EF<14			
n(%)	0	2 (1.7)	
EF=14–25			
n(%)	25 (20.8)	83 (69.2)	
EF±25			
n(%)	95 (79.2)	35 (29.2)	

IIEF, International Index of Erectile Function.
P value was significant if less than 0.05.

Table 2: Associations of prolactin with clinical parameters among cases group

	Prolactin			
	Mean±SD	Median	Range	*P* value
No fever	5.63	5.63	5.63	0.303
Fever	20±13.9	15.83	4.89–93.62	
No admission	19.5±12.8	15.60	4.89–55.79	0.628
Admission	20.9±16.5	16.23	7.83–93.62	
Noninfected partner	18.7±12.2	14.78	4.89–55.79	0.547
Infected partner	20.4±14.5	15.83	5.11–93.62	

Table 3: Associations of testosterone with clinical parameters among cases group

	Testosterone			
	Mean±SD	Median	Range	*P* value
No fever	2.9±0	2.9	2.9	0.811
Fever	2.6±1.1	2.38	1.32–5.72	
No admission	2.6±1.1	2.27	1.32–5.72	0.380
Admission	2.8±1.2	2.50	1.32–5.60	
Noninfected partner	2.6±1.1	2.59	1.32–5.72	0.970
Infected partner	2.6±1.1	2.27	1.32–5.60	

When compared with the control group, cases had significantly reduced mean orgasmic function, sexual desire, intercourse satisfaction, total sexual satisfaction, and overall IEF (Table 4). PRL correlated significantly positively with age and significantly negatively with erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction.Although there was a significant positive correlation between tT and erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction, there was a significant negative correlation between tT and age (Table 5). Receiver operating characteristic curves of PRL and tT, on the contrary, were used to predict EF less than 25 following COVID-19 recovery. PRL and tT demonstrated moderate accuracy, with area under the curves of 0.772 and 0.739, respectively. Sensitivity was 65.7% and specificity was 76.5% at the optimum PRL cutoff value of 11.6ng/ml. Sensitivity was 62.9% and specificity was 69.4% at the best cutoff value of tT (2.9ng/ml). Other aspects of performance are displayed (Fig.1).

In univariate analysis, younger age, lower PRL, and higher tT were related with higher IIEF. On incorporating relevant covariates from univariate analysis into multivariate analysis, only lower PRL and greater tT were found to be predictors of increased IIEF after COVID-19 recovery (Table 6).

Table 4: Compression of results of International Index of Erectile Function questionnaire among studied groups

	Control (N=120)	Cases (N=120)	*P* value
Orgasmic function			
Range	6–10	4–10	<0.001
Mean±SD	8.64±1.17	7.51±1.57	
Sexual desire			
Range	6–10	4–10	<0.001
Mean±SD	8.6±1.10	7.5±1.46	
Intercourse satisfaction			
Range	9–15	5–15	<0.001
Mean±SD	12.90±1.50	11.45±2.04	
Overall satisfaction			
Range	6–10	4–10	<0.001
Mean±SD	8.63±0.98	7.55±1.52	
IEFF			
Range	48–72	37–67	<0.001
Mean±SD	64.7±6.4	56.4±7.4	

Table 5: Correlation between hormonal assay and different function domain of International Index of Erectile Function scale

	Prolactin		Testosterone	
	rs	*P* value	*rs*	*P* value
Erectile function	-0.370	<0.001	0.302	<0.001
Orgasmic function	-0.190	0.003	0.241	<0.001
Sexual desire	-0.188	0.004	0.273	<0.001
Intercourse satisfaction	-0.340	<0.001	0.244	<0.001
Overall satisfaction	-0.187	0.004	0.263	<0.001

rs, correlation coefficient.

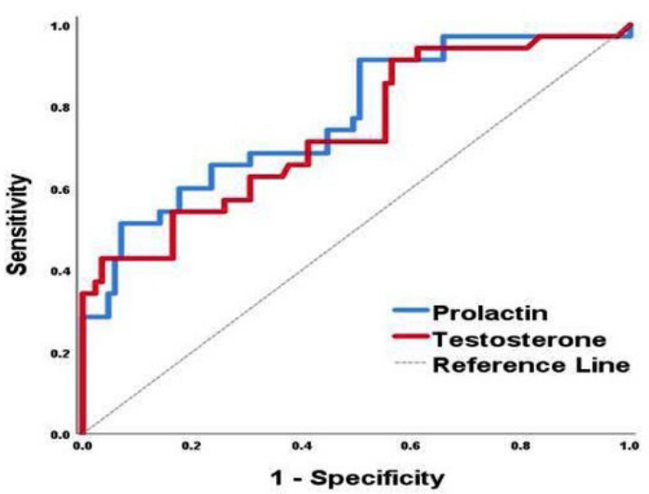

Fig. 1: ROC curve of prolactin and testosterone for prediction of EF <25 after COVID-19 recovery

Table 6: Regression analysis for prediction of International Index of Erectile Function after coronavirus disease 2019 recovery

	Univariate		Multivariate	
	B	*P* value	B	*P* value
Age	-0.191	0.025	-0.105	0.205
Residence	0.530	0.702		
Education	-0.282	0.828		
Fever	-6.613	0.376		
Admission	1.146	0.451		
Infected partner	0.358	0.814		
Prolactin	-0.164	0.001	-0.107	0.031
Testosterone	2.204	<0.001	1.649	0.007

B, regression coefficient.

Statistical analysis

Statistical Package for the Social Sciences (SPSS Version 25.0. IBM Corp. 2017, Armonk, NY.USA) was used to analyze the data.To determine normality, the Kolmogorov–Smirnov test was applied. For parametric numerical data, mean and SD were employed, whereas median and range were used for nonparametric data. Student t test was used to assess significance of the difference between two means. For a nonparametric variable, the Mann–Whitney test was used. The $\chi 2$ and Fisher's exact tests were employed to investigate the association between qualitative variables.

Cronbach's alpha was used to examine the internal consistency of the questionnaire. To assess the strength of association between quantitative variables, correlation analysis tests were used. Receiver operating characteristic curve was used to evaluate the sensitivity and specificity of diagnostic values. Univariate and multivariate regression linear regression analyses were used for prediction of risk factors.

DISCUSSION

Viral infections such as COVID-19 can disrupt the endocrine system by activating inflammatory and cytokine pathways that stimulate the hypothalamic–pituitary–adrenal axis[4].

Sertoli and Leydig cells significantly express the enzyme ACE2, which has been identified as the key receptor of COVID-19, implying that SARS-CoV-2 infection can result in subclinical testicular damage with subsequent hypogonadism and compromised testicular functions[5]. Furthermore, COVID-19 particles and ACE2 were found in the penile vascular endothelial cells. Consequently, erectile function may be negatively affected[6].

Based on this understanding, the current study was performed to discover the underappreciated effect of COVID-19 infection on men's sexual functions in a sample of Egyptians. When compared with the control group, our findings demonstrated significantly higher PRL and significantly lower tT in the examined patients (Table 1). These findings are consistent with those of Kumar *et al.*[7], who found hyperprolactinemia in 21 (8.5%) individuals with no relationship to COVID-19 severity. Similarly, we found no association between PRL and clinical data such as fever, hospitalization, or partner infection (Table 2), implying that hyperprolactinemia may be stress induced.

Circulating tT levels were observed to be increased at 7-month follow-up compared with hospital admission levels, but more than 50% of recovered men still had low circulating tT levels[8]. SARS-CoV-2 infection is linked to sparse intratubular cells with vacuolated Sertoli cells as well[9].

Our findings revealed no relationship between tT and COVID-19 clinical data (Table 3). On the contrary, a low tT level was thought to be a predictor of sickness severity[10]. Furthermore, despite equal comorbidities at presentation, it was proposed that males with lower baseline tT levels may experience worse outcomes as a result of COVID-19[11].

Xu *et al.*[12] discovered that COVID-19 cases exhibited normal tT, FSH, and LH levels with no significant differences when compared with controls. Estradiol and PRL levels, on the contrary, were both above the top limit of normal ranges.

The current study found that mean EF scores in cases were significantly lower than in controls. EF scores (14–25) were present in 83/120 (69.2%) of the patients, with two cases having EF less than 14 (Table 1). These findings could be explained by the hypothesis that virus-induced endothelial cell dysfunction is the cause of erectile dysfunction[13].

The present study revealed significantly reduced mean orgasmic function, sexual desire, mean overall IEF, and mean overall sexual pleasure in terms of sexual functioning in recovered men compared with controls (Table 4). This is consistent with the findings of Rabies[14], who found that

more than 80% of the individuals under examination had diminished erectile function (85% were self-limited, and <5% were irreversible).Yang *et al.*[15] reported increased severity of anxiety, depression, and stress perception during COVID-19 infection, and both sexes showed an increase in sexual dysfunctions.

Furthermore, we found significant negative correlations between PRL and sexual functions in reverse to tT (Table 5). By demonstrating significant associations between IIEF-5 scores, PRL values, and the Trauma Symptoms Checklist (TSC-40), Fiala *et al.*[16] came to the conclusion that, rather than reducing tT levels, hyperprolactinemia may cause sexual dysfunction through the stress effect. According to Brotto *et al.*[17], during the pandemic, there was a stronger desire for solo sexual activity and a decrease in relationship satisfaction. On the contrary, Maggi *et al.*[18] discovered that an acute, but not chronic, PRL increase is associated with facilitated sexual activity.

According to Karagöz *et al.*[19] and Yang *et al.*[15], the IIEF-15 scores were significantly lower during the pandemic than before. During COVID-19 infection, the severity of anxiety, depression, and stress perception increased, and both sexes showed an increase in sexual dysfunctions.

The prediction of EF less than 25 following COVID-19 recovery was analyzed using regression analysis in relation to different parameters. High PRL and low tT were found to be the only significant predictors for lower IIEF rating following COVID-19 recovery (P =0.001 and P<0.001, respectively) (Table 6). In the same context, Sansone *et al.*[20] mentioned that decreased testosterone secretion from the affected testis could be an indirect negative effect of COVID-19 on ED. Nevertheless, clinical manifestations of COVID-19 infection in the studied patients did not show significant predictive value in contrary to Saad *et al.*[21] who concluded that COVID-19 severity was a significant independent factor (P=0.008).

LIMITATION OF THE STUDY

Our study's limitations included a small sample size, being a single-center study, and only discussing the short-term sexual effects of COVID-19.

CONCLUSION

According to the findings, it is considered that COVID-19 can have a deleterious effect on several elements of sexual functioning in men via a variety of variables. The fundamental mechanism is still not fully understood.

CONFLICT OF INTEREST

There are no conflicts of interest.

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