










Erectile dysfunction after COVID-19 infection: A cross-sectional study in a male sample from Brazil

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ABSTRACT

Introduction: COVID-19 infection may cause erectile dysfunction due to local viral infection and impairing mental health. **Objective:** To analyze the erectile function in Brazilian sample patients during pandemics with and without COVID-19 infection and compare with results from a sample obtained before the pandemic. **Methods:** Internet survey with epidemiologic questions, data on COVID-19 infection, and the International Index for Erectile Function (IIEF). Patients were divided into those with and without infections. A control group with results obtained before the pandemic was also included. **Results:** Four hundred twenty-two males were studied 210 with data obtained before the pandemic; 208 with data obtained during the pandemic (84 with COVID-19 infection and 124 without). Patients with COVID-19 infection had worse results of IIEF than those without (in the pandemics and before pandemics) with $p=0.01$ and used more sexual stimulants ($p=0.02$). The results were worse in the first month after the infection. **Conclusion:** Patients with COVID-19 infection had impairment in erectile function that is more severe in the first month after infection.

Keywords: erectile dysfunction; COVID-19; pandemic; men.

INTRODUCTION

The COVID-19 pandemic has imposed severe losses in the physical and mental health of the general population secondary to fear and anxiety added to the infection's consequences in all segments of the body. The extra burn was imposed on men, as males are more vulnerable to the infection and exhibit poorer prognosis than females¹. So, it is not surprising that the male sexual health may be affected during this period. Psychological and/or physical problems may play a role in this context. Negative behavioral changes connected to emotional and social well-being impairment are factors that affect sexual desire². Important levels of endogenous cortisol in chronic stress situations can decrease monadic steroids and adrenal androgens that are known to have facilitating effects on sexual desire and genital arousal³⁻⁵. In addition, SARS-CoV-2, although a respiratory virus that affects the lungs, is capable of infecting other tissues. Reproductive organs express the angiotensin-converting enzyme (ACE)-2 receptor that promotes viral access to the cell⁶ and SARS COV 2 virus is found infecting spermatogonia, spermatids, Sertoli, and Leydig cells⁷ although the consequences of such infection are still unknown.

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Herein, the male sexual performance in COVID-19-infected males was studied comparing it with the performance of those without infection during and before pandemics.

METHODS

Ethical issues

This study was approved by the local committee of ethics in research from University *Positivo*, protocol number 4.770.674.

Study design and participants.

This work had a convenience sample that included males who answered the online survey from August 02, 2021, to November 14, 2021. The internet survey was conducted through social media (Facebook®, Instagram®, and WhatsApp® groups) to males over 18 years of age. The study was publicized in groups of men (groups of companies, civil construction, drivers, health professionals, etc.) randomly, via social media. The researchers tried to distribute the questionnaire so that men of different ages and levels of education participated, to reduce biases and have homogeneous groups for comparison.

After consent, the participant answered questions that included epidemiological data, COVID-19 infection and treatment data, comorbidities, and questions from the International Index of Erectile Function-5 (IIEF-5). The diagnosis of COVID-19 was self-declared. Cases with COVID-19 responded that they had been confirmed by PCR tests (nasopharyngeal swab). The presence of comorbidities was self-reported.

The IIEF-5 is an instrument to grade the electrical function that has five questions answered through a Likert scale. Results lower than 7 points were considered compatible with severe dysfunction; those with values between 8 and 11, with moderate, values from 12 to 16 as slight to moderate dysfunction, values from 17 to 21 as slight dysfunction, and higher than 21 as normal⁸.

For comparison purposes, three groups were listed: a) Men who responded to the IIEF-5 questionnaire before the pandemic, b) Men who answered the questionnaire and reported having had COVID-19, c) Men who claimed not to have had COVID-19 after about 12 months of the beginning of the pandemic in Brazil.

Men in the healthy group responded to the IIEF-5 for more than 12 months, before the onset of the pandemic, and were part of a control group from a previous study⁹ on erectile dysfunction from the same study group.

Statistical analysis

Obtained data was collected in contingency and frequency tables. Chi-squared tests were used to compare nominal data (demographic data, presence of comorbidities, and use of sexual stimulants among the three groups: before the pandemic, in the

pandemics with COVID-19 infection and the pandemics without COVID-19 infection) and categorical data (classification of IIEF-5 results and change in the perception of sexual performance prior and after pandemic in the three groups). The Mann-Whitney test was used to compare two groups of numerical data (comparison of age; comparison of IIEF-5 values in individuals with COVID-19 infection with and without hospitalization and comparison of IIEF-5 values of individuals with more than 1 month from COVID-19 infection with those before pandemics).

The Kruskal-Wallis test followed by Dunn's multiple comparison test was used to compare values of IIEF-5 scores in the three studied groups and in the COVID-19 infection group classified according to the time from infection). Data distribution was judged by the Shapiro-Wilk test. The adopted significance was 5%. Comparison tests were performed using GraphPad Prism version 8.0.0 for Windows, GraphPad Software, San Diego, California USA (www.graphpad.com).

RESULTS

Four hundred twenty-two males responded to the Internet survey, being n=210 of them considered as a control group (data obtained before the pandemic); n=208 of them answered the questions during the pandemic, of which 84/208 (40.3%) have had COVID-19 infection and 124/208 (59.6%) did not. Among those with infection, 71 (84.5%) had done confirmatory tests for the infection and 6/84 (7.1%) needed hospital admission.

Table 1 has details on epidemiological and comorbidities data. The three groups (controls, during the pandemic without infection, and pandemics with infection) were paired for age.

Among individuals with COVID-19 infection, 5.9% have had this infection less than 1 month before the survey, 28.6% in 2-4 months, 35.7% in 5-8 months, 21.4% in 9 to 12 months, and 8.3% more than 1 year.

According to the IIEF results, 38.2% of individuals with COVID-19 infection had some degree of sexual dysfunction while this happened in 28.2% of those studied in the pandemic but without infection. In males studied before the pandemic, the frequency of some degree of dysfunction was 31.9%. The results of IIEF according to the studied groups and degree of erectile dysfunction are shown in Figure 1, which displays those males with COVID-19 infection had worse performance than the other two groups (p=0.01).

The median value of IIEF in the group with COVID-19 infection was 20.7±5.3, the median value obtained in the group during pandemics and without COVID-19 infection was 22.2±3.4 and the median value of individuals before the pandemic was 21.8±3.8 (p=0.03; one way ANOVA). Tukey's multiple comparison test showed that the difference was between the group of COVID-19 infection and the group during pandemics and without infection (adjusted value p=0.03).

When the individuals from the sample with COVID-19 infection were asked to compare their sexual performance before and after infection, the results of Figure 2A were obtained.

Among the group of patients with COVID-19 infection, when the IIEF from patients that needed hospitalization (median value of 20; IQR=10.7 - 20.5) was compared to those without it (median value of 23; IQR=19.7 - 25.0), p=0.02 was obtained.

Figure 2B shows the values of IIEF of the group with COVID-19 infection according to the time elapsed after infection. The values in the first month were lower than the others although not statistically significant.

The comparison of IIEF-5 values in individuals with COVID-19 more than 1 month from the infection (median of 23; IQR=20.0-25.0) with individuals without infection during pandemics

Table 1: Epidemiological and comorbidities data in the studied sample.

	During pandemics n=208		Before pandemics n=210	p value
	With COVID-19 infection - n=84	Without COVID-19 infection - n=124		
Median age (IQR) - years	26 (22-38)	24 (21-35)	24 (22-33)	0.22
Fixed partner - n (%)	54 (62.4)	88 (70.9)	139 (66.1)	0.54
Tobacco exposure - n (%)	10 (11.9)	17 (13.7)	25 (11.9)	0.55
Arterial hypertension - n (%)	7 (8.3)	5 (4.0)	12 (5.7)	0.42
Depression - n (%)	4 (4.7)	16 (12.9)	11 (5.2)	0.02
Diabetes - n (%)	1 (1.1)	2 (1.6)	NA	0.99
Use of sexual stimulant - n (%)	19 (22.6)	12 (9.6)	NA	0.01 (*)

(*) OR = 2.7; 95%CI = 1.2 - 5.9.
n=number; IQR=interquartile range; NA= not available.

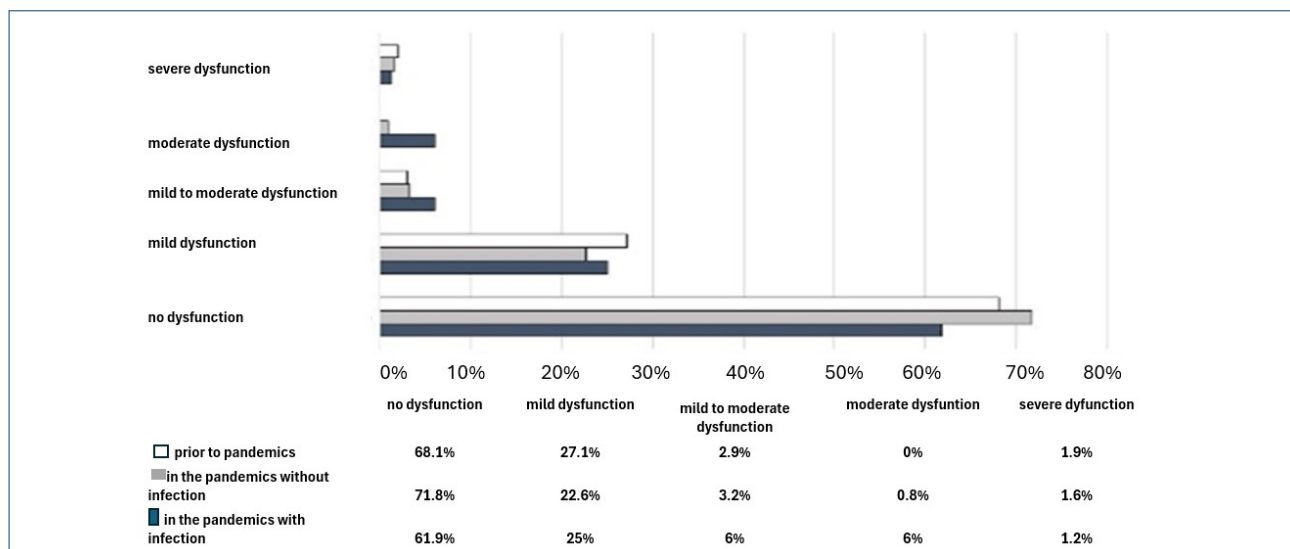


Figure 1: International Index of Erectile Function (IIEF) in males prior and post-pandemics (n=422).

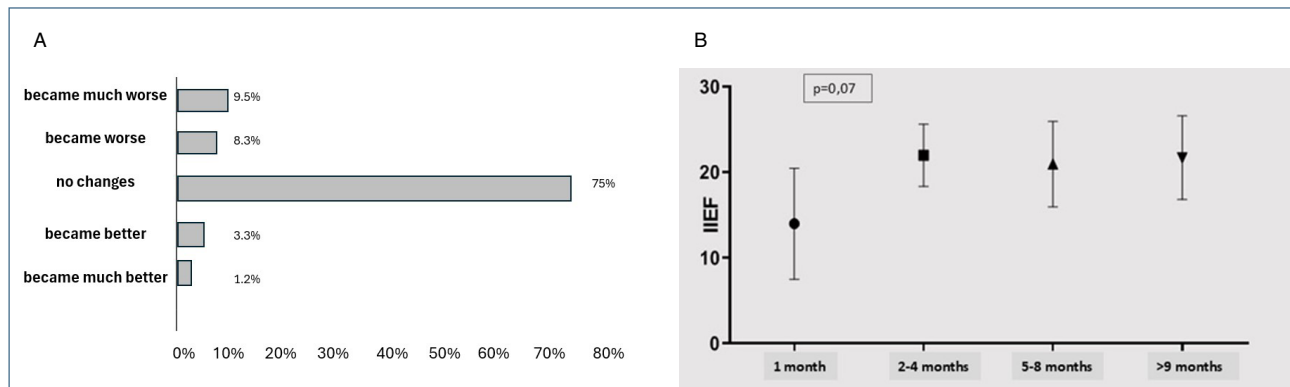


Figure 2: (A) Comparison of sexual performance pre and post COVID-19 infection. (B) International Index of Erectile Function (IIEF) values according to time after infection.

(median=23; IQR=21.0-25.0) and individuals before pandemic (median of 23; IQR= 20.7- 24.0) showed no differences ($p=0.29$).

DISCUSSION

The results of the present analysis have shown that individuals with COVID-19 infection have a lower median level of IIEF-5 when compared to the results from males studied before pandemics and during the pandemics but without infection. They also have a high use of sexual stimulants. The result was even worse in those who needed hospitalization. Nevertheless, the present findings show a milder effect of this infection on sexual performance than those found by Harirugsakul et al.¹⁰ who studied 153 men from Thailand with COVID-19 infection and observed that 67% of them had erectile dysfunction, mostly mild. However, these latter authors did not include a control group. Sansone et al.¹¹ found a prevalence nearer to the presently found, of 28% while studying an Italian sample. Salar et al.¹², studying 83 patients with confirmed COVID-19 infection concluded that the infection caused deterioration in previously existing erectile dysfunction regardless of infection's severity.

These same authors could not find changes in the testosterone, follicle-stimulating, luteinizing, and prolactin hormone levels before and after the disease.

One hypothesis to explain the sexual function decline is that the psychological distress resulting from the lockdown imposed by the disease would help to impair sexual function. During the COVID-19 outbreak, high rates of psychiatric disorders such as depression and anxiety disorders were reported¹³ and the association of sexual dysfunction with mental health has been documented in several other studies¹⁴⁻¹⁸.

Another explanation for impairment in erectile function after COVID-19 infection is that there is an organic effect resulting from viral invasion in gonadal tissues. As already mentioned, ACE-2 receptors are highly expressed in reproductive organs favoring local invasion. Kresch et al.¹⁹ studying tissue obtained from patients undergoing penile prosthesis for severe erectile dysfunction after COVID-19 infection, found viral particles near penile vascular endothelial cells confirming local infection and reduced

endothelial nitric oxide synthase expression (a marker of endothelial function) in the corpus cavernosum suggesting that endothelial cell dysfunction is an active player. Moreover, ischemia after microvascular injury secondary to coagulopathy offers an additional explanation²⁰. Low testosterone levels may be another important contributor to this setting. Testicular involvement by COVID-19 has been confirmed in autopsy results and may result in impaired production of testosterone which is a modulator of male sexual response²¹.

Additionally, some studies have shown that pro-inflammatory cytokines such as interleukin (IL)-1, IL-6, and TNF alpha, which are increased during this infection, diminish testosterone secretion by acting both centrally (hypothalamus and pituitary) and peripherally (testicles)^{22,23}.

The values of IIEF were worse in patients just after the infection (1 month) and thereafter they remained stable, suggesting an acute effect of the infection in this context.

This work is limited by its design which uses electronic data collection. So, all obtained data was based on the patient's information without any laboratory proof. It also has a limited number of participants as it used a convenience sample. Another observation must be made; the results on erectile dysfunction between the group of COVID-19 infection and the group during pandemics and without infection were statistically significant, but the difference in absolute values of IIEF was just around 2 units. This may not be translated into clinically significant differences. Prospective studies are necessary to obtain such information. On the other hand, it has the advantage of showing no long-term impact of COVID-19 infection on erectile function. Moreover, questionnaires about sexuality should have more reliable answers when conducted anonymously and online than if they were applied in person.

Conclusion

The present study shows that patients with COVID-19 infection had impairment in erectile function that was statistically more severe in the first month after infection. Further studies are needed to understand the clinical impact of this finding.

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