



## Prevalence of Sexual Long COVID (SLC) in Egypt: A Single Institute Study

Ahmed Said Zaghoul MD<sup>1</sup>, Abd El Rahman Mahmoud ElNashar MD<sup>1</sup>, Hossam Refaat Eldebs MD<sup>1</sup>, Sameh Fayek Gamal, El Din MD<sup>1</sup>, Hany Mohammed Saad MD<sup>2</sup>, Shady Zaki Said MD<sup>1</sup>

<sup>1</sup>Andrology, Sexology & Sexually Transmitted Infections (STIs) Department, Kasr Al-Ainy Faculty of Medicine, Cairo University, Cairo, Egypt.

<sup>2</sup>Department of Andrology, Faculty of Medicine, Suez Canal University, Ismailia, Egypt.

\*Corresponding Author Email: [Hossamrefaat39388@postgrad.kasralainy.edu.eg](mailto:Hossamrefaat39388@postgrad.kasralainy.edu.eg)

Article History	Abstract
Received: 06 June 2023 Revised: 05 September 2023 Accepted: 27 September 2023	<p><b>Objectives:</b> we conducted a cross section study to assess the prevalence and severity of ED among COVID-19 survivors presenting to andrology outpatients' clinics, Kasr AlAiny hospital, faculty of medicine, Cairo university.</p> <p><b>Materials and Methods:</b> a total of 1000 COVID-19 survivors were screened for ED using validated Arabic version of the international index of erectile function (ArIIEF-5) during the period between Jan 2022 till Jan 2023. All patients were previously diagnosed with positive PCR for COVID-19 infection at least 3 months before the time of data collection.</p> <p><b>Result:</b> we found that the prevalence of ED among COVID-19 survivors were 11.4%, mild ED in 7%, moderate in 3.2% and severe ED in 1.2%, severity of ED was not associated with demographic, clinical, laboratory and penile duplex characteristics.</p> <p><b>Conclusion:</b> severity of ED among COVID-19 survivors showed no statistically significant association with demographics, depression, anxiety, penile duplex findings and hormonal disturbances.</p> <p><b>Key words:</b> erectile dysfunction, covid-19, endothelial function, anxiety, depression</p>
CC License CC-BY-NC-SA 4.0	

### 1. Introduction

In March 2020, world health organization has declared severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection emerged in Wuhan City, Hubei Province, China as a global pandemic, officially named as coronavirus disease 2019 (COVID-19) (1). Currently, COVID-19 is estimated to have infected 770,778,396, including 6,958,499 deaths as per WHO reported September 2023 (2).

The post-acute sequelae of SARS-CoV-2 infection known as long covid is a significant matter of clinical and public health importance. It is characterized by the persistence, recurrence, or emergence of symptoms or illnesses that manifest 30 days or more following the initial infection (3, 4).

Erectile dysfunction (ED) serves as a sign for endothelial dysfunction in cardiovascular disorders, has been documented as one of the symptoms associated with COVID-19, either immediately or in the long term. The correlation between ED and COVID-19, as observed in real-world scenarios, aligns with the pathophysiological pathways that link ED, endothelial dysfunction, and COVID-19 (5).

Based on existing evidence, it has been observed that SARS-CoV-2 infiltrates endothelial cells by utilizing ACE2 and transmembrane protease serine 2 (TMPRSS2). This invasion of endothelial cells has been extensively studied as a significant characteristic of the immunological hyper-response, which is linked to more severe outcomes in cases of acute COVID-19 (6).

Consequently, there is a prevailing expectation that the organs impacted by SARS-CoV-2 are likely to experience effects from long COVID. This correlation offers a reasonable rationale for the many clinical manifestations observed in individuals with long COVID (7, 8).

## **2. Materials and methods**

We screened 1000 patients who presented to andrology outpatient clinics, Kasr AlAiny hospital, Cairo university during the period between Jan 2022 till Jan 2023. ED was diagnosed using a validated Arabic version of the international index of erectile function (ArIIEF-5) (9). All patients were previously diagnosed with positive PCR for COVID-19 infection at least 3 months before the time of data collection.

Nasal and pharyngeal swab specimens were used to obtain a sample for quantitative reverse transcriptase polymerase chain reaction (PCR) to diagnose covid-19 positivity in all cases. Any recovered patient from COVID-19 for at least 3 months and complaining of ED was eligible for inclusion in the present study, while any recovered patients with history of ED prior to COVID-19 or suffering from any chronic illness as hypertension, diabetes, or ischemic heart diseases was excluded.

All patients were subjected to detailed medical history taking, thorough physical examination, patients were questioned about any previous instances of testicular symptoms during or after infection with COVID-19. All patients filled ArIIEF-5, General Anxiety Disorder-7 (GAD-7) questionnaire (10), Patient Health Questionnaire-9 as a screening tool for depression (11), and penile duplex.

The researchers employed a color Doppler ultrasound machine equipped with a linear array probe ranging from 7.5 to 10 MHz. The Doppler parameters were tuned specifically for the purpose of measuring velocity following pharmaco-stimulation. It was crucial to have a Doppler angle that was below 60 degrees. The patient was positioned in a supine posture, and the duplex probe was placed on the ventral portion of the penis. The longitudinal axis of the probe was aligned parallel to the longitudinal axis of the penis.

Prior to administering 20 grams of PGE1 to the penis, the diameter of the cavernosal arteries was assessed. Following the administration of an intra-cavernosal injection, an assessment was conducted on the penis to ascertain the extent and duration of penile stiffness. During the duration of the investigation, the quality of the erection was evaluated as per Broderick & Arger recommendations.

### **Statistical analysis**

The statistical package for the social sciences (SPSS) version 22 software (IBM SPSS Inc., Chicago, IL, USA) was used for data entry, coding, and analysis of the collected data. The Friedman test was used as a test of significance for the variables that were examined, and the Kalmagarov-Smirnov test was used to confirm that the distribution of variables was normal. The results were deemed to be significant at the 5% level.

## **3. Results and Discussion**

we enrolled 1000 COVID-19 survivors who sought medical consultations in the andrology department of Kasr AlAiny hospital, Cairo university, prevalence of ED was 11.4%, 7% were mild ED, 3.2% were moderate ED and 1.2% were severe ED according to validated Arabic version of the international index of erectile function (ArIIEF-5).

Comparison of demographics characteristics according to severity of ED showed no statistically significant differences in age, spouse age, duration of marriage, smoking, past medical and surgical history between study groups with p values >0.05. Forty patients were diagnosed with depression and 40 patients were diagnosed with anxiety.

There was no statistically significant difference between study groups according to severity of ED in terms of total testosterone and prolactin levels, as well as penile duplex findings, and prevalence of anxiety and depression.

Penile duplex showed no abnormalities across all studied groups, as well, the Corpus Caverosum which showed normal diameter at the time of presentation.

		Severity of ED						P value
		Mild		Moderate		Severe		
		Median	25th-75th	Median	25th-75th	Median	25th-75th	
Age in years		33	29-38	34.5	30-40	35.5	33-43.5	0.188
Spouse age		28	25-33	31	26-38	29.5	27-40	0.154
Duration of marriage		6	2-10	8	4-14.5	8	2.5-10	0.068
		Count	%	Count	%	Count	%	
Special habits	Non-smoker	45	64.3%	14	43.8%	8	66.7%	0.124
	Smoker	25	35.7%	18	56.3%	4	33.3%	
Medical history	Free	68	97.1%	30	93.8%	12	100.0%	0.872
	HCV	1	1.4%	1	3.1%	0	0.0%	
	Hypothyroidism	1	1.4%	1	3.1%	0	0.0%	
Surgical history	BIL.HLO	2	2.9%	0	0.0%	0	0.0%	0.910
	Free	60	85.7%	30	93.8%	12	100.0%	
	hernia repair	1	1.4%	0	0.0%	0	0.0%	
	hernioplasty	1	1.4%	0	0.0%	0	0.0%	
	hydrocelectomy	1	1.4%	0	0.0%	0	0.0%	
	orchidopexy	0	0.0%	1	3.1%	0	0.0%	
	Piles	1	1.4%	0	0.0%	0	0.0%	
	TESE	4	5.7%	1	3.1%	0	0.0%	
Depression	No	49	70.0%	18	56.3%	7	58.3%	0.354
	Yes	21	30.0%	14	43.8%	5	41.7%	
Anxiety	No	47	67.1%	22	68.8%	5	41.7%	0.201
	Yes	23	32.9%	10	31.3%	7	58.3%	
Testicular size	Normal	26	37.1%	13	40.6%	6	50.0%	0.923
	Moderate	38	54.3%	17	53.1%	5	41.7%	
	Small	6	8.6%	2	6.3%	1	8.3%	
Penile examination	Normal	70	100.0%	32	100.0%	12	100.0%	NA
Penile	Normal	52	74.3%	18	56.3%	4	33.3%	0.055

duplex clinical response	E4	6	8.6%	4	12.5%	2	16.7%	
	E5	12	17.1%	10	31.3%	6	50.0%	
		Median	25th-75th	Median	25th-75th	Median	25th-75th	
Total testosterone (ng/dL)		5.35	4.6-6.3	5.4	4.55-6.35	4.8	4.1-6.92	0.953
Prolactin ng/ml		10.75	8.2-12.9	10.5	8.9-12.75	11.35	11.05-14.05	0.290
Penile duplex (PSV 5 min.)		58	58-58	42	39-45	61.5	51-72	0.223
Penile duplex (PSV 20 min.)		57	57-57	39.5	37-42	63	51-75	0.233
Penile duplex (RT. Cavernous diameter)		0.5	0.5-0.5	0.5	0.4-0.5	0.6	0.5-0.6	0.368
Penile duplex (LT. Cavernous diameter)		0.5	0.5-0.5	0.5	0.4-0.5	0.6	0.5	0.386
<b>PSV: peak systolic volume, LT: left, RT: right</b>								

After declaration of WHO COVID-19 as a pandemic in March 2020 (12), there had been a large body of evidence that associate the COVID-19 infection with endothelia dysfunction and its correlation with ED among male patients (5, 13, 14).

Other causes as depression, mental health issues and social distancing were associated with increased prevalence of ED worldwide (15), specifically among patients who were diagnosed with severe COVID or admitted to ICU (16, 17).

Erectile dysfunction pathophysiology in COVID-19 patients had been explained in various theories, COVID-19 was found to impact the physiological processes associated with penile erection including vasculogenic, neurogenic, and endocrine pathways (18, 19).

Endothelial dysfunction, subclinical hypogonadism, and poor pulmonary hemodynamics are factors that may contribute to the development of erectile dysfunction (ED) in individuals affected by COVID-19 (20, 21).

COVID-19-associated vasculopathy has the potential to adversely affect the delicate vascular network of the penis, which may lead to compromised erectile efficiency (22, 23).

A systematic review that includes 204 peer-reviewed studies, encompassing a total of 2092 individuals diagnosed with COVID-19 and 1138 control subjects. The findings of this systematic review and meta-analysis indicate a significant correlation between SARS-CoV-2 infection and a decline in levels of total testosterone (TT), as well as a detrimental impact on sperm production (24).

Additionally, social distancing and stay at home policy has led to relationship strain, besides, job losses and economic problems which yielded higher prevalence of anxiety and depression (25).

In the present study we found that prevalence of sexual long covid affected 11.4% of the included patients, our findings were consistent with many reported in turkey, Duran et al., reported that erectile dysfunction was 8.7% among COVID-19 survivors.

An Italian online survey study by Sansone et al., reported higher prevalence of ED among COVID-19 survivors accounting for 28%, logistic regression showed that previous COVID-19 infection was associated with 5.66 odds ratio of having ED (14).

A survey was conducted on 612 Chinese men. The findings revealed that a proportion of self-reported decline in erectile function or ejaculation control ability were 8.4% and 8.5%. Additionally, 31.9%

and 17.9% respectively, exhibited decreased scores on the International Index of Erectile Function-5 (IIEF-5) questionnaire or increased scores on the premature ejaculation diagnostic tool. They reported that ED was mainly associated with higher scores of PHQ-9 and GAD-7 and higher prevalence of anxiety and depression (26), which was aligned with the findings of the current study.

A case control study showed that patients with long covid syndrome who have recovered from mild to moderate COVID-19 pneumonia at least 3 months ago, exhibited lower total and free testosterone levels, and higher LH levels compared to control group (27).

In general, long COVID encompasses a range of problems that have the potential to adversely affect erectile function leading to sexual long covid through various pathogenetic processes (28). Consequently, addressing these complications may necessitate customized therapeutic approaches. Thorough examination and effective administration by a specialist in sexual medicine are thus very necessary. Furthermore, there is a justified demand for further study on this subject matter.

We believe that the limitations of the current study are relatively low incidence of erectile dysfunction among the screened population, lower number of patients with severe and moderate ED, finally, being a single institute study may limit the generalizability of our findings across the whole region.

#### 4. Conclusion

Erectile dysfunction is a prevalent andrological condition observed in individuals with long covid syndrome. The etiology of this condition is complex, including a combination of endocrine and psychological factors.

#### References:

1. Shi Y, Wang G, Cai XP, Deng JW, Zheng L, Zhu HH, et al. An overview of COVID-19. *Journal of Zhejiang University Science B*. 2020;21(5):343-60.
2. World Health O. Therapeutics and COVID-19: living guideline, 13 January 2023. World Health Organization; 2023.
3. Davis HE, Assaf GS, McCorkell L, Wei H, Low RJ, Re'em Y, et al. Characterizing long COVID in an international cohort: 7 months of symptoms and their impact. *EClinicalMedicine*. 2021;38.
4. Danesh V, Arroliga AC, Bourgeois JA, Boehm LM, McNeal MJ, Widmer AJ, et al. Symptom clusters seen in adult COVID-19 recovery clinic care seekers. *Journal of General Internal Medicine*. 2023;38(2):442-9.
5. Kaynar M, Gomes ALQ, Sokolakis I, Gül M. Tip of the iceberg: erectile dysfunction and COVID-19. *International Journal of Impotence Research*. 2022;34(2):152-7.
6. Jin Y, Ji W, Yang H, Chen S, Zhang W, Duan G. Endothelial activation and dysfunction in COVID-19: from basic mechanisms to potential therapeutic approaches. *Signal transduction and targeted therapy*. 2020;5(1):293.
7. Perico L, Benigni A, Casiraghi F, Ng LFP, Renia L, Remuzzi G. Immunity, endothelial injury and complement-induced coagulopathy in COVID-19. *Nature reviews Nephrology*. 2021;17(1):46-64.
8. Crook H, Raza S, Nowell J, Young M, Edison P. Long covid-mechanisms, risk factors, and management. *BMJ (Clinical research ed)*. 2021;374:n1648.
9. Shamloul R, Ghanem H, Abou-zeid A. Validity of the Arabic version of the sexual health inventory for men among Egyptians. *Int J Impot Res*. 2004;16(5):452-5.
10. Toussaint A, Hüsing P, Gumz A, Wingefeld K, Härter M, Schramm E, et al. Sensitivity to change and minimal clinically important difference of the 7-item Generalized Anxiety Disorder Questionnaire (GAD-7). *Journal of affective disorders*. 2020;265:395-401.
11. Levis B, Benedetti A, Thombs BD. Accuracy of Patient Health Questionnaire-9 (PHQ-9) for screening to detect major depression: individual participant data meta-analysis. *BMJ (Clinical research ed)*. 2019;365:11476.
12. Jee Y. WHO international health regulations emergency committee for the COVID-19 outbreak. *Epidemiology and health*. 2020;42.
13. Harirugsakul K, Wainipitapong S, Phannajit J, Paitoonpong L, Tantiwongse K. Erectile dysfunction after COVID-19 recovery: A follow-up study. *Plos one*. 2022;17(10):e0276429.
14. Sansone A, Mollaioli D, Ciocca G, Colonnello E, Limoncin E, Balercia G, et al. "Mask up to keep it up": Preliminary evidence of the association between erectile dysfunction and COVID-19. *Andrology*. 2021;9(4):1053-9.
15. Fu Q, Ge J, Xu Y, Liang X, Yu Y, Shen S, et al. The evolution of research on depression during COVID-19: A visual analysis using Co-Occurrence and VOSviewer. *Frontiers in public health*. 2022;10:1061486.

16. Pons S, Fodil S, Azoulay E, Zafrani L. The vascular endothelium: the cornerstone of organ dysfunction in severe SARS-CoV-2 infection. *Critical care*. 2020;24(1):1-8.
17. Tuttle E, Wisecup C, Lemieux E, Wang X, Modrykamien A. Critically ill patients boarding in the emergency department and the association with intensive care unit length of stay and hospital mortality during the COVID-19 pandemic. *Proceedings (Baylor University Medical Center)*. 2022;35(2):145-8.
18. Ahamed J, Laurence J. Long COVID endotheliopathy: Hypothesized mechanisms and potential therapeutic approaches. *The Journal of Clinical Investigation*. 2022;132(15).
19. Pelle MC, Zaffina I, Lucà S, Forte V, Trapanese V, Melina M, et al. Endothelial dysfunction in COVID-19: potential mechanisms and possible therapeutic options. *Life*. 2022;12(10):1605.
20. Sansone A, Jannini E. COVID-19 and erectile dysfunction: endothelial dysfunction and beyond. *The World Journal of Men's Health*. 2021;39(4):820-1.
21. Malik J, Younus F, Iftikhar I, Usman M. Love in the time of COVID-19: a scoping review on male sexual health. *Journal of Community Hospital Internal Medicine Perspectives*. 2021;11(4):496-500.
22. Flaumenhaft R, Enjyoji K, Schmaier AA. Vasculopathy in COVID-19. *Blood, The Journal of the American Society of Hematology*. 2022;140(3):222-35.
23. Becker RC. COVID-19-associated vasculitis and vasculopathy. *Journal of thrombosis and thrombolysis*. 2020;50:499-511.
24. Corona G, Vena W, Pizzocaro A, Pallotti F, Paoli D, Rastrelli G, et al. Andrological effects of SARS-Cov-2 infection: a systematic review and meta-analysis. *Journal of endocrinological investigation*. 2022;45(12):2207-19.
25. Hsieh T-C, Edwards NC, Bhattacharyya SK, Nitschelm KD, Burnett AL. The epidemic of COVID-19-related erectile dysfunction: a scoping review and health care perspective. *Sexual Medicine Reviews*. 2022;10(2):286-310.
26. Fang D, Peng J, Liao S, Tang Y, Cui W, Yuan Y, et al. An Online Questionnaire Survey on the Sexual Life and Sexual Function of Chinese Adult Men During the Coronavirus Disease 2019 Epidemic. *Sexual medicine*. 2021;9(1):100293.
27. Al-kuraishy HM, Al-Gareeb AI, Alarfaj SJ, Al-Akeel RK, Faidah H, El-Bouseary MM, et al. Long COVID and risk of erectile dysfunction in recovered patients from mild to moderate COVID-19. *Scientific Reports*. 2023;13(1):5977.
28. Sansone A, Mollaioli D, Limoncin E, Ciocca G, Băc NH, Cao TN, et al. The Sexual Long COVID (SLC): Erectile Dysfunction as a Biomarker of Systemic Complications for COVID-19 Long Haulers. *Sex Med Rev*. 2022;10(2):271-85.
29. Guo, Y., & Korteweg, C. (2020). Pathology and pathogenesis of severe acute respiratory syndrome. *The American Journal of Pathology*, 177(4), 1750-1755.
30. Li, D., Jin, M., Bao, P., Zhao, W., & Zhang, S. (2020). Clinical characteristics and results of semen tests among men with coronavirus disease 2019. *JAMA Network Open*, 3(5), e208292.
31. Sansone, A., Mollaioli, D., Ciocca, G., Colonnello, E., Limoncin, E., Balercia, G., ... & Jannini, E. A. (2021). "Mask up to keep it up": Preliminary evidence of the association between erectile dysfunction and COVID-19. *Andrology*, 9(4), 1053-1059.
32. Salonia, A., Corona, G., Giwercman, A., Maggi, M., Minhas, S., Nappi, R. E., ... & Serefoglu, E. C. (2021). SARS-CoV-2, testosterone and frailty in males (PROTEGGIMI): A multidimensional research project. *Andrology*, 9(1), 19-22.
33. Rastrelli, G., Di Stasi, V., Inglese, F., Beccaria, M., Garuti, M., Di Costanzo, D., ... & Maggi, M. (2021). Low testosterone levels predict clinical adverse outcomes in SARS-CoV-2 pneumonia patients. *The Journal of Sexual Medicine*, 18(1), 206-214.
34. Silva, F. T., & Leite, M. L. (2021). Erectile dysfunction in patients with COVID-19: Pathogenesis, prevalence, and relevance. *The Journal of Sexual Medicine*, 18(10), 1754-1758.
35. Montague, D. K., & Jarow, J. P. (2005). Guideline on the pharmacologic management of premature ejaculation. *The Journal of Urology*, 173(4), 1880-1882.
36. Balachandar, V., Mahalaxmi, I., Subramaniam, M., Kaavya, J., Senthil Kumar, N., & Laldinmawii, G. (2020). Follow-up studies in COVID-19 recovered patients—Is it mandatory? *Science of the Total Environment*, 729, 139021.
37. Chen, Y., Guo, Y., Pan, Y., & Zhao, Z. J. (2020). Structure analysis of the receptor binding of 2019-nCoV. *Biochemical and Biophysical Research Communications*, 525(1), 135-140.
38. Salonia, A., Corona, G., Giwercman, A., Maggi, M., Minhas, S., Nappi, R. E., ... & Serefoglu, E. C. (2021). SARS-CoV-2, testosterone and frailty in males (PROTEGGIMI): A multidimensional research project. *Andrology*, 9(1), 19-22.

39. Sansone, A., Mollaioli, D., Ciocca, G., Limoncin, E., Colonnello, E., Vena, W., ... & Jannini, E. A. (2021). Addressing male sexual and reproductive health in the wake of COVID-19 outbreak. *Journal of Endocrinological Investigation*, 44(2), 223-231.
40. Li, G., Tang, D., Song, B., Wang, C., & Qunshan, S. (2020). Erectile dysfunction and its severity are significantly correlated with the severity of COVID-19. *The Canadian Journal of Urology*, 27(5), 10350-10355.
41. Rastrelli, G., Di Stasi, V., Inglese, F., Beccaria, M., Garuti, M., Di Costanzo, D., ... & Maggi, M. (2021). Low testosterone levels predict clinical adverse outcomes in SARS-CoV-2 pneumonia patients. *Andrology*, 9(1), 88-98.
42. Duran, M., Gür, M., Yıldız, Ş. Ş., Demirtaş, Ş., Akın, Ş., Özdemir, O., ... & Korkmaz, L. (2021). High rate of erectile dysfunction in COVID-19 patients. *The Aging Male*, 1-6.
43. Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., ... & Cao, B. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet*, 395(10223), 497-506.