Received: 18 September 2021 | Revised: 23 October 2021 | Accepted: 29 October 2021

DOI: 10.1111/and.14308

ORIGINAL ARTICLE

WILEY

Predictive factors of erectile dysfunction in Egyptian individuals after contracting COVID-19: A prospective case–control study

Hany Mohammed Saad[1] | Sameh Fayek GamalEl Din[2] | Osama Mohamed Elbokl[2] | Ahmed Adel[2]

[1]Department of Andrology, Faculty of Medicine, Suez Canal University, Ismailia, Egypt

[2]Department of Andrology, Faculty of Medicine, Cairo University, Cairo, Egypt

Correspondence
Sameh Fayek GamalEl Din, Department of Andrology and STDs Kasr Al-Ainy, Faculty of medicine Cairo University, Al-Saray Street, El Manial, Cairo 11956, Egypt.
Email: samehfayek@hotmail.com

Abstract

This study aimed to screen healthy individuals who contracted COVID-19 for erectile dysfunction (ED) and to determine the potential risk factors that can predict ED in these individuals. One hundred and seven cases versus 90 controls agreed to participate in the study. Two structured interviews with 1 month interval were conducted. All participants were evaluated by the validated Arabic version of the international index of erectile function (IIEF-5) and assessment of the psychological state by Hamilton depression rating scale (HDRS). Interestingly, the study had demonstrated a significant difference in mean testosterone level between cases and controls (3.91 ± 2.31, 5.04 ± 2.22, $p < 0.001$ respectively). Additionally, the study had demonstrated a significant difference in mean IIEF-5 score between cases and controls (22.63 ± 2.79, 23.54 ± 1.26, $p < 0.041$ respectively). Moreover, there were significant differences in mean anxiety and stress scores of the cases before and after COVID-19 (4.95 ± 4.03, 6.19 ± 3.55, $p = 0.022$, 12.75 ± 9.98, 15.30 ± 7.42, $p = 0.024$ respectively). A multiple logistic regression model for predicting ED occurrence post-COVID-19 had revealed that smoking, baseline IIEF-5 score and COVID-19 severity ($p = 0.022$, $p = 0.017$, $p = 0.021$, $p = 0.009$, $p = 0.008$ respectively) were the only significant independent variables.

KEYWORDS
COVID-19, erectile dysfunction, Hamilton depression rating scale, international index of erectile function-5, smoking

1 | INTRODUCTION

An overwhelming health concern about cases suffering from acute respiratory distress was first discovered in Wuhan, Hubei Province, China, in December (2019). These cases turned out to be affected by corona virus disease 2019 (COVID-19) with substantial casualties. The aetiology of COVID-19 had been determined as a novel corona virus, now known as severe acute respiratory syndrome corona virus 2 (SARS-CoV-2; Ahn et al., 2020; Dhama et al., 2020). Corona viruses possess large (~30-kb) single-stranded, positive-sense RNA genomes that are divided into a 50 two-thirds and a 30 third (Ge et al., 2020; Lai et al., 2020). The first two-thirds code for 2 large polyproteins that are proteolytically cleaved into non-structural proteins essential for the production of new viral genetic material. The rest codes for structural proteins and carry the accessory genes that produce virions and alter the host response (Ge et al., 2020; Lai et al., 2020). Unfortunately, asymptomatic or minimally symptomatic patients affected by COVID-19 could silently transfer the

disease to too many people, leading to an exponential increment in its casualties (Mostafa, 2021). Interestingly, overwhelming evidence had shown that 'silent' asymptomatic forms of COVID-19 were associated with subclinical microvascular involvement resulted in long-term cardiovascular sequel in these patients (Liu et al., 2020; Long et al., 2020; Oran & Topol, 2020; Vittori et al., 2020). The onset of more severe forms of COVID-19 provoked endothelial dysfunction that was associated with different comorbidities (Bernard et al., 2021). Remarkably, oral epithelial cells and other respiratory tract areas are the most susceptible sites to viral entry as they have an extensive expression of angiotensin-converting enzyme 2 (ACE2; Xu, Zhong, et al., 2020; Xu, Chen, et al., 2020; Zhang et al., 2020; Zhou et al., 2020).

Thus, COVID-19 is an endothelial disease that causes systemic manifestations as a result of tissue ischaemia that occurs from changes in endothelial thrombotic/fibrinolytic balance (Libby & Luscher, 2020). Consistently, apoptosis of the endothelial cells destroys the pulmonary microvascular and alveolar epithelial cells resulting in vascular leakage and alveolar oedema that ends in hypoxia with subsequent multiple organ failure (Ye et al., 2020). Moreover, many of the co-factors expressed by endothelial cells are used by COVID-19 to invade host cells (Pons et al., 2020). It is worth mentioning that erectile dysfunction (ED) had been recognized as a benchmark of endothelial disease (Guay, 2007; Jannini, 2017). Consequently, a hypothetical link between ED and COVID-19 had been hypothesized (Sansone et al., 2021). Another potential link is shared risk factors for ED and COVID-19 (Caci et al., 2020; Mahase, 2020; Mollaioli et al., 2020; Romanelli et al., 2010). Moreover, adult male Leydig cells secrete ACE2 which substantiated the possibility of testicular damage following infection (Douglas et al., 2004). A state of subclinical testicular dysfunction can occur in COVID-19 suggesting impaired steroidogenesis (Ma et al., 2020; Pal & Banerjee, 2020). We aimed in the current prospective case–control study to screen healthy individuals who contracted COVID-19 for ED. Consequently, we would be able to determine the potential risk factors that can predict ED in these individuals.

2 | MATERIAL AND METHODS

The current case–control study was conducted on healthy men contracted COVID-19. They were recruited from specialized units at Kasr Al-Ainy hospital in addition to other specialized hospitals set for isolating these patients from January (2021) to May (2021).

The study was performed in accordance with the Helsinki Declaration guidelines (2013) after receiving institutional review board approval. All participants provided a written informed consent. COVID-19 was confirmed after using the reverse transcription polymerase chain reaction (RT-PCR) test of pharyngeal and nasal swabs. The severity of COVID-19 was determined following the guidelines stated by Xu, Zhong, et al. (2020). According to these guidelines, the frame is characterized by aetiology, epidemiology, pathology, clinical characteristics, diagnostic criteria, classification, clinical warning indicates severe and critical cases, differential diagnosis, case finding and reporting, treatment, criteria for discontinuation and discharge, transfer principles, nosocomial infection control (7th version). The infectious agent is COVID-19 (4th version) which may also be asymptomatic (5th version). The condition may be transmitted by respiratory droplet and contact transmission (4th version) in addition to aerosols transmission (6th version) or transmission by contact with faeces and urine (7th version). Finally, the susceptible population is the crowd (4th to 7th versions).

2.1 | Inclusion criteria of the patients

Healthy males aged 20–40 years and sexually active that tested COVID-19 positive was invited to join the study. They should finish the management protocol and had been discharged at least 2 weeks prior to joining the study.

2.2 | Exclusion criteria of the patients

All patients with endocrinal diseases, neurological diseases, prostatic diseases, pelvic trauma or spinal cord injury, peyronie's disease or curvature, alcoholics, metabolic syndrome and chronic illnesses (diabetes mellitus, hypertension, liver disease, renal failure, cardiovascular disease) were excluded.

2.3 | Inclusion criteria of the controls

Ninety age-matched married potent men were included. They did not contract COVID-19 and were attending our clinic for fertility potential checkup.

Eight hundred and eighty men were admitted to the aforementioned hospitals during the period where the study was conducted. After exclusion criteria, 300 cases remained and only 107 cases agreed to participate in the study as patients versus 90 controls. All cases were contacted via telephone 2 weeks after their discharge from the isolation hospital. They were evaluated for the first time within 1 month after being diagnosed of having COVID-19 as some cases needed to stay at the isolation hospital for 1 to 2 weeks. One month afterwards, they were evaluated for the second time. They were exposed to full history taking, clinical examination and evaluation of potency by the validated Arabic version of the international index of erectile function (Shamloul et al., 2004). They were also assessed for the psychological state by Hamilton depression rating scale (HDRS; Hamilton, 1960). Finally, a morning 5 cc blood was withdrawn from the participants for total testosterone evaluation after a 12 h overnight fasting. Total testosterone was measured once using fully automated electrochemiluminescent immunoanalyzer Cobas 400 (Normal value: 1.88–8.8 ng/ml).

2.4 | Statistical analysis

Collected data were coded, entered and analysed using statistical package for social sciences (SPSS) version 25 software (IBM SPSS Inc.) program for analysis. The Kolmogorov–Smirnov was used to verify the normality of the distribution of variables and accordingly paired *t* tests were used as test of significance for the studied variables in patients group. Mann–Whitney test was used as test of significance for comparing cases and control groups. Chi-square test for association between categorical variables was used. The significance of the obtained results was judged at the 5% level.

3 | RESULTS

Socio-demographic data of the cases are listed in Tables 1 and 2. The majority of the cases maintained good erection post-COVID-19 (Table 3). The current study had shown a significant difference in mean IIEF-5 score of the cases before and after COVID-19 (23.53 ± 1.21, 22.63 ± 2.79, $p < 0.001$ respectively; Table 4). The study had also shown a significant difference in mean depression score of the cases before and after COVID-19 (7.08 ± 3.47, 8.47 ± 5.88, p 0.014 respectively; Table 4). Moreover, there were significant differences in mean anxiety and stress scores of the cases before and after COVID-19 (4.95 ± 4.03, 6.19 ± 3.55, $p = 0.022$, 12.75 ± 9.98, 15.30 ± 7.42, $p = 0.024$ respectively; Table 4). Interestingly, the study had demonstrated a significant difference in mean testosterone level between cases and controls (3.91 ± 2.31, 5.04 ± 2.22, $p < 0.001$ respectively; Table 5). Also, there was a significant negative correlation between serum testosterone in cases and COVID-19 severity ($r = -0.226$, $p = 0.019$).

Additionally, the study had demonstrated a significant difference in mean IIEF-5 score between cases and controls (22.63 ± 2.79, 23.54 ± 1.26, $p < 0.041$ respectively; Table 5). Conversely, the smoking status between cases and controls did not show any statistical significance (Table 5). A multiple logistic regression model for post-COVID-19 ED had revealed that smoking, baseline IIEF-5 score and COVID-19 severity were the only significant independent variables ($p = 0.022$, $p = 0.017$, $p = 0.021$, $p = 0.009$, $p = 0.008$ respectively; Table 6). As shown in table (6), the EXP (β) for the odds ratio (OR) evaluation with a 95% degree of confidence had demonstrated that the probability of post-COVID-19 ED in smokers was 7.643 times more likely compared to non-smokers. Furthermore, a 1% drop in the baseline IIEF-5 score determined a decrease in OR for post-COVID-19 ED with 60.5%. The probability of post-COVID-19 ED in moderate and severe cases was 28.402 and 47.793 times more likely compared to mild cases respectively. Conversely, there was non-significant association between post-COVID ED and age and baseline HDRS score ($p > 0.05$).

4 | DISCUSSION

Recently, several studies had demonstrated that sexual quality of life and function might be negatively affected due to COVID-19 (Li et al., 2020; Panzeri et al., 2020; Sansone et al., 2021). The current study had shown that COVID-19 was associated with ED in healthy males and low testosterone level. Consistently, Duran et al. (2021) and Sansone et al. (2021) have revealed similar findings. On the other hand, Omar et al. (2021) had shown that majority of their male cases did not report ED during COVID-19 lockdown.

Notably, we excluded plausible causes of ED as diabetes mellitus, hypertension and cardiovascular diseases as ED is a well-recognized interface of systemic comorbidity (Jannini, 2017). Thus, our study asserted the tight link between contracting COVID-19 and ED. In addition, our study had revealed that probability of ED occurrence post-COVID-19 in moderate and severe cases was 28.402 and 47.793 times more likely compared to mild cases respectively. The findings of our study can be seen in line with the aetiopathological mechanisms relating ED, endothelial disease and COVID-19 together (Sansone et al., 2021). Furthermore, a very recent study had detected COVID-19 virus in the penis after initial infection in humans as well as widespread endothelial cell dysfunction from COVID-19 infection (Kresch et al., 2021). The present study had demonstrated significant differences in serum testosterone between cases and controls. Moreover, the study had revealed a significant negative correlation between serum testosterone in cases and COVID-19 severity. The low testosterone associated with COVID-19 can be explained by the facts that adult Leydig cells express ACE2 that is used by the virus as an entry point to the cells using the transmembrane protease serine 2 (TMPRSS2; Oran & Topol, 2020). Thus, testicular involvement occurs due to COVID-19 infection through ACE2 (Douglas et al., 2004). Changes in the coagulation status leading to development of ischaemia at a microvascular level with subsequent

TABLE 1 Socio-demographic data of the cases

Cases ($n = 107$)	Minimum	Maximum	Mean	SD
Age (years)	24	40	32.66	±4.83
Marriage duration (years)	1	15	5.92	±3.94
IIEF-5				
Before COVID-19	22	25	23.53	±1.21
After COVID-19	4	25	22.63	±2.79
Total Testosterone (ng/ml)	1	8.90	3.90	±2.31

Note: Key: IIEF-5 = the validated Arabic version of the international index of erectile function.

testicular injury could be added as another theory for testicular damage in COVID-19 (Flaifel et al., 2021). Further, a state of hypergonadotropic hypogonadism can independently occur as a result of testicular damage (Kadihasanoglu et al., 2021; Ma et al., 2020; Okcelik, 2021; Pal & Banerjee, 2020; Rastrelli et al., 2021). It is well known that testosterone modulates endothelial function (Isidori et al., 2014).

Thus, impaired testosterone secretion from the affected testis could be added as an indirect negative impact of COVID-19 on ED (Sansone et al., 2014). Moreover, our study had revealed significant differences in scores of HDRS between cases and controls in addition to the cases pre and post-COVID-19. This finding could be expected by the negative impact of the relatively high mortality inflicted be COVID-19 together with the stressful lock down measures (Omar et al., 2021). The current study did not reveal any role for depression and anxiety as potential predictive factors of ED in healthy individuals after contracting COVID-19. This finding could be seen in agreement with that reported by Omar et al. (2021) who found that majority of their male cases were not suffering from ED and no sexual relationship stress despite the fact that they were suffering from depression and anxiety. The current study is one of the first to highlight the potential role of smoking and baseline IIEF-5 score and severity of COVID-19 to predict the occurrence of ED in healthy individuals post-COVID-19. Several observational studies had demonstrated an evidence based medicine about a positive dose–response association between quantity and duration of smoking and risk of ED (Cao et al., 2014). Thus, smoking can make healthy individuals post-COVID-19 at a higher risk of suffering from ED following recovery from this pandemic. Additionally, Sansone et al. (2021) had demonstrated a link between ED, endothelial disease and COVID-19 together. Furthermore, Oran and Topol (2020) had revealed that low testosterone was associated with COVID-19. In the same context, our study had revealed a significant negative correlation between serum testosterone in cases and COVID-19 severity. Thus, severe COVID-19 infection can make healthy individuals post-COVID-19 at a higher risk of suffering from ED following recovery from this pandemic.

Finally, baseline ED was found to be one of the predictors of ED in healthy individuals post-COVID-19 as 29 individuals out of 107 were suffering from ED ranging from mild-to-severe ED. Thus, the presence of mild ED can make healthy individuals post-COVID-19 at a higher risk of suffering from ED following recovery from this pandemic as 24 cases out of 27 cases were suffering from mild ED. Also, this finding asserts the negative impact of COVID-19 on ED. Admittedly, there are several weakness points in our study. Firstly, lack of full data for the

TABLE 2 Frequency and distribution of smoking and main complaint and severity of COVID-19 among cases

Cases (n = 107)		Frequency (n)	Percentage (%)
Smoking	Smokers	45	42.1
	Non-smokers	62	57.9
Main complaint of COVID-19	Cough	62	57.9
	Diarrhoea	42	39.3
	Fever	51	47.7
	Muscle pain	39	36.4
	Loss of smell	36	33.6
	Loss of taste	36	33.6
	Sore throat	18	16.8
	Headache	13	12.1
	Fatigue/ weakness	101	94.4
COVID-19 severity	Mild	53	49.5
	Mod	35	32.7
	Severe	19	17.8

TABLE 3 Shows the frequency and distribution of erectile dysfunction (ED) severity among the cases post-COVID-19 according to the international index of erectile function

	Frequency	Percentage (%)
No ED (22–25)	78	72.9
Mild ED (17–21)	24	22.42
Mild-to-moderate ED (12–16)	3	3
Moderate ED (8–11)	1	1
Severe ED (1–7)	1	1

Cases (n = 107)		Mean	SD	p value
IIEF-5	Before COVID-19	23.53	±1.21	<0.001
	After COVID-19	22.63	±2.79	
Depression	Before COVID-19	7.08	±3.47	0.014
	After COVID-19	8.47	±5.88	
Anxiety	Before COVID-19	4.95	±4.03	0.022
	After COVID-19	6.19	±3.55	
Stress	Before COVID-19	12.75	±9.98	0.024
	After COVID-19	15.30	±7.42	

TABLE 4 Comparison between the validated Arabic version of the international index of erectile function (IIEF) and Hamilton depression rating scale (HDRS) scores before and after COVID-19 infection in the cases

Key: IIEF-5 = the validated Arabic version of the international index of erectile function.

TABLE 5 Comparison between age and total testosterone and the validated Arabic version of the international index of erectile function and smoking between cases and controls

			Minimum	Maximum	Mean	SD	*p* value
Age (years)	Cases		24	40	32.66	±4.83	0.903
	Controls		22	40	32.76	±5.02	
Testosterone (ng/ml)	Cases		1	8.90	3.90	±2.31	<0.001
	Controls		1.80	9.20	5.04	±2.22	
IIEF-5	Cases before COVID-19		22	25	23.53	±1.21	0.945
	Controls		22	25	23.54	±1.26	
	Cases after COVID-19		4	25	22.63	±2.79	0.041
	Controls		22	25	23.54	±1.26	
				Frequency	Percentage (%)		*p* value
Smoking	Cases	Smokers		45	42.1		0.736
		Non-smokers		62	57.9		
	Controls	Smokers		40	44.4		
		Non-smokers		50	55.6		

Key: IIEF-5 = the validated Arabic version of the international index of erectile function.

TABLE 6 Logistic regression analysis of the correlation between the study variables and the occurrence of erectile dysfunction in patients who contracted COVID-19

	β	SE	Wald	*p* value	Exp (*β*)	95% CI for EXP(*β*)	
Age (years)	0.007	0.095	0.005	0.942	1.007	0.836	1.213
Smoking (smokers)	2.034	0.889	5.232	0.022	7.643	1.338	43.656
Smoking (Non-smokers)							
Baseline IIEF-5	−0.930	0.388	5.737	0.017	0.395	0.184	0.845
Different grades of COVID-19							
Mild			7.689	0.021			
Moderate	3.346	1.287	6.762	0.009	28.402	2.280	353.834
Severe	3.867	1.454	7.071	0.008	47.793	2.764	826.337
HDRS							
Depression	−0.081	0.103	0.622	0.430	0.922	0.753	1.128
Anxiety	0.103	0.091	1.274	0.259	1.108	0.927	1.325
Stress	0.043	0.038	1.241	0.265	1.044	0.968	1.125

Key: IIEF-5 = the validated Arabic version of the international index of erectile function, HDRS = Hamilton depression rating scale.

participants' sexual function before contracting COVID-19. Although we used the validated Arabic index during the first visit for this purpose, yet, it covered only the preceding 4 weeks before joining the study. The same limitation can also be seen for serum testosterone and scores of HDRS. Lack of long-term follow-up as well is one of the limitations. Finally, it should be stated that a one point drop in IIEF-5 score although statistically significant is not clinically significant.

5 | CONCLUSION

Severe COVID-19 can be associated with ED in healthy individuals after recovery as a complication. Interestingly, smoking and baseline erectile status as well as COVID-19 severity are the most important predictive factors of ED in these individuals.

ACKNOWLEDGEMENT

This study was self-funded.

CONFLICT OF INTEREST

All authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Hany Mohammed Saad https://orcid.org/0000-0001-9319-5027

Sameh Fayek GamalEl Din https://orcid.org/0000-0003-1918-5132

REFERENCES

Ahn, D., Shin, H., Kim, M., Lee, S., Kim, H. S., Myoung, J., Kim, B. T., & Kim, S. J. (2020). Current status of epidemiology, diagnosis, therapeutics, and vaccines for novel coronavirus disease 2019 (COVID-19). *Journal of Microbiology and Biotechnology*, *30*, 313–324. https://doi.org/10.4014/jmb.2003.03011

Bernard, I., Limonta, D., Mahal, L. K., & Hobman, T. C. (2021). Endothelium infection and dysregulation by SARS-CoV-2: Evidence and caveats in COVID-19. *Viruses*, *13*(1), 29.

Caci, G., Albini, A., Malerba, M., Noonan, D. M., Pochetti, P., & Polosa, R. (2020). COVID-19 and obesity: Dangerous liaisons. *Journal of Clinical Medicine*, *9*(8), 2511. https://doi.org/10.3390/jcm9082511

Cao, S., Gan, Y., Dong, X., Liu, J., & Lu, Z. (2014). Association of quantity and duration of smoking with erectile dysfunction: A dose-response meta-analysis. *The Journal of Sexual Medicine*, *11*(10), 2376–2384. https://doi.org/10.1111/jsm.12641

Dhama, K., Khan, S., Tiwari, R., Sircar, S., Bhat, S., Malik, Y. S., Singh, K. P., Chaicumpa, W., Bonilla-Aldana, D. K., & Rodriguez-Morales, A. J. (2020). Coronavirus disease 2019 COVID-19. *Clinical Microbiology Reviews*, *33*, e00028–20.

Douglas, G. C., O'Bryan, M. K., Hedger, M. P., Lee, D. K., Yarski, M. A., Smith, A. I., & Lew, R. A. (2004). The novel angiotensin-converting enzyme (ACE) homolog, ACE2, is selectively expressed by adult Leydig cells of the testis. *Endocrinology*, *145*(10), 4703–4711. https://doi.org/10.1210/en.2004-0443

Duran, M. B., Yildirim, O., Kizilkan, Y., Tosun, C., Cirakoglu, A., Gultekin, M. H., Gul, U., Altan, M., Sah, C., Hasirci, E., Ceyhan, E., Ongun, S., & Turunc, T. (2021). Variations in the number of patients presenting with andrological problems during the coronavirus disease 2019 pandemic and the possible reasons for these variations: A multicenter study. *Sexual Medicine*, *9*, 100292. https://doi.org/10.1016/j.esxm.2020.100292

Flaifel, A., Guzzetta, M., Occidental, M., Najari, B. B., Melamed, J., Thomas, K. M., & Deng, F. M. (2021). Testicular changes associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *Archives of Pathology and Laboratory Medicine*, *145*(1), 8–9. https://doi.org/10.5858/arpa.2020-0487-LE

Ge, H., Wang, X., Yuan, X., Xiao, G., Wang, C., Deng, T., Yuan, Q., & Xiao, X. (2020). The epidemiology and clinical information about COVID-19. *European Journal of Clinical Microbiology and Infectious Diseases*, *39*, 1011–1019. https://doi.org/10.1007/s10096-020-03874-z

Guay, A. T. (2007). ED2: Erectile dysfunction = endothelial dysfunction. *Endocrinology and Metabolism Clinics of North America*, *36*(2), 453–463.

Hamilton, M. (1960). A rating scale for depression. *Journal of Neurology Neurosurgery and Psychiatry*, *23*, 56–62. https://doi.org/10.1136/jnnp.23.1.56

Isidori, A. M., Buvat, J., Corona, G., Goldstein, I., Jannini, E. A., Lenzi, A., Porst, H., Salonia, A., Traish, A. M., & Maggi, M. (2014). A critical analysis of the role of testosterone in erectile function: From pathophysiology to treatment – A systematic review. *European Urology*, *65*(1), 99–112. https://doi.org/10.1016/j.eururo.2013.08.048

Jannini, E. A. (2017). SM = SM: The interface of systems medicine and sexual medicine for facing non-communicable diseases in a genderdependent manner. *Sexual Medicine Reviews*, *5*(3), 349–364.

Kadihasanoglu, M., Aktas, S., Yardimci, E., Aral, H., & Kadioglu, A. (2021). SARSCoV-2 pneumonia affects male reproductive hormone levels: A prospective, cohort study. *The Journal of Sexual Medicine*, *18*(2), 256–264. https://doi.org/10.1016/j.jsxm.2020.11.007

Kresch, E., Achua, J., Saltzman, R., Khodamoradi, K., Arora, H., Ibrahim, E., Kryvenko, O. N., Almeida, V. W., Firdaus, F., Hare, J. M., & Ramasamy, R. (2021). COVID-19 endothelial dysfunction can cause erectile dysfunction: Histopathological, immunohistochemical, and ultrastructural study of the human penis. *The World Journal of Men's Health*. https://doi.org/10.5534/wjmh.210055

Lai, C. C., Shih, T. P., Ko, W. C., Tang, H. J., & Hsueh, P. R. (2020). Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease 2019 (COVID-19): The epidemic and the challenges. *International Journal of Antimicrobial Agents*, *55*, 105924. https://doi.org/10.1016/j.ijantimicag.2020.105924

Li, G., Tang, D., Song, B., Wang, C., Qunshan, S., Xu, C., Geng, H., Wu, H., He, X., & Cao, Y. (2020). Impact of the COVID-19 pandemic on partner relationships and sexual and reproductive health: Cross-sectional, online survey study. *Journal of Medical Internet Research*, *22*(8), e20961. https://doi.org/10.2196/20961

Libby, P., & Luscher, T. (2020). COVID-19 is, in the end, an endothelial disease. *European Heart Journal*, *41*(32), 3038–3044. https://doi.org/10.1093/eurheartj/ehaa623

Liu, P. P., Blet, A., Smyth, D., & Li, H. (2020). The science underlying COVID-19: Implications for the cardiovascular system. *Circulation*, *142*(1), 68–78. https://doi.org/10.1161/CIRCULATIONAHA.120.047549

Long, Q. X., Tang, X. J., Shi, Q. L., Li, Q., Deng, H. J., Yuan, J., Hu, J. L., Xu, W., Zhang, Y., Lv, F. J., Su, K., Zhang, F., Gong, J., Wu, B., Liu, X. M., Li, J. J., Qiu, J. F., Chen, J., & Huang, A. L. (2020). Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. *Nature Medicine*, *26*(8), 1200–1204. https://doi.org/10.1038/s41591-020-0965-6

Ma, L., Xie, W., Li, D., Shi, L., Mao, Y., Xiong, Y., Zhang, Y., & Zhang, M. (2020). Efect of SARS-CoV-2 infection upon male gonadal function: A single center-based study. *MedRxiv*, *200*, 37–67.

Mahase, E. (2020). Covid-19: Why are age and obesity risk factors for serious disease? *BMJ*, *371*, m4130. https://doi.org/10.1136/bmj.m4130

Mollaioli, D., Ciocca, G., Limoncin, E., Di Sante, S., Gravina, G. L., Carosa, E., Lenzi, A., & Jannini, E. A. F. (2020). Lifestyles and sexuality in men and women: The gender perspective in sexual medicine. *Reproductive Biology and Endocrinology*, *18*(1). 10. https://doi.org/10.1186/s12958-019-0557-9

Mostafa, T. (2021). Could oral phosphodiesterase 5 inhibitors have a potential adjuvant role in combating coronavirus disease 2019 infection? *Sexual Medicine Reviews*, *9*, 15e22.

Okcelik, S. (2021). COVID-19 pneumonia causes lower testosterone levels. *Andrologia*, *53*(1), e13909. https://doi.org/10.1111/and.13909

Omar, S. S., Dawood, W., Eid, N., Eldeeb, D., Munir, A., & Arafat, W. (2021). Psychological and sexual health during the COVID-19 pandemic in Egypt: Are women suffering more. *Sexual Medicine*, *9*, 100295. https://doi.org/10.1016/j.esxm.2020.100295

Oran, D. P., & Topol, E. J. (2020). Prevalence of asymptomatic SARS-CoV-2 infection: A narrative review. *Annals of Internal Medicine*, *173*(5), 362–367. https://doi.org/10.7326/M20-3012

Pal, R., & Banerjee, M. (2020). COVID-19 and the endocrine system: Exploring the unexplored. *Journal of Endocrinological Investigation*, *43*(7), 1027–1031. https://doi.org/10.1007/s40618-020-01276-8

Panzeri, M., Ferrucci, R., Cozza, A., & Fontanesi, L. (2020). Changes in sexuality and quality of couple relationship during the COVID-19 lockdown. *Frontiers in Psychology*, *11*, 565823. https://doi.org/10.3389/fpsyg.2020.565823

Pons, S., Fodil, S., Azoulay, E., & Zafrani, L. (2020). The vascular endothelium: The cornerstone of organ dysfunction in severe SARS-CoV-2

infection. *Critical Care*, *24*(1), 353. https://doi.org/10.1186/s13054-020-03062-7

Rastrelli, G., Di Stasi, V., Inglese, F., Beccaria, M., Garuti, M., Di Costanzo, D., Spreafico, F., Greco, G. F., Cervi, G., Pecoriello, A., Magini, A., Todisco, T., Cipriani, S., Maseroli, E., Corona, G., Salonia, A., Lenzi, A., Maggi, M., De Donno, G., & Vignozzi, L. (2021). Low testosterone levels predict clinical adverse outcomes in SARS-CoV-2 pneumonia patients. *Andrology*, *9*(1), 88–98. https://doi.org/10.1111/andr.12821

Romanelli, F., Sansone, A., & Lenzi, A. (2010). Erectile dysfunction in aging male. *Acta Biomedica*, *81*(Suppl 1), 89–94.

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*, 1–7. https://doi.org/10.1111/andr.13003

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. https://doi.org/10.1007/s40618-020-01350-1

Sansone, A., Romanelli, F., Gianfrilli, D., & Lenzi, A. (2014). Endocrine evaluation of erectile dysfunction. *Endocrine*, *46*(3), 423–430.

Shamloul, R., Ghanem, H., & Abou-zeid, A. (2004). Validity of the Arabic version of the sexual health inventory for men among Egyptians. *International Journal of Impotence Research*, *16*(5), 452–455. https://doi.org/10.1038/sj.ijir.3901248

Vittori, A., Lerman, J., Cascella, M., Gomez-Morad, A. D., Marchetti, G., Marinangeli, F., & Picardo, S. G. (2020). COVID-19 pandemic acute respiratory distress syndrome survivors: Pain after the storm? *Anesthesia and Analgesia*, *131*(1), 117–119. https://doi.org/10.1213/ANE.0000000000004914

World Medical Association. (2013). World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human subjects. *JAMA*, *310*(20), 2191–2194.

Xu, H., Zhong, L., Deng, J., Peng, J., Dan, H., Zeng, X., Li, T., & Chen, Q. (2020). High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. *International Journal of Oral Science*, *12*, 8.

Xu, Y., Chen, Y., & Tang, X. (2020). Guidelines for the diagnosis and treatment of coronavirus disease 2019 (COVID-19) in China. *Global Health & Medicine*, *2*(2), 66–72. https://doi.org/10.35772/ghm.2020.01015

Ye, Q., Wang, B., & Mao, J. (2020). The pathogenesis and treatment of the 'Cytokine Storm' in COVID-19. *Journal of Infection*, *80*, 607–613. https://doi.org/10.1016/j.jinf.2020.03.037

Zhang, H., Penninger, J. M., Li, Y., Zhong, N., & Slutsky, A. S. (2020). Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: Molecular mechanisms and potential therapeutic target. *Intensive Care Medicine*, *46*(4), 586–590. https://doi.org/10.1007/s00134-020-05985-9

Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z., Xiang, J., Wang, Y., Song, B., Gu, X., Guan, L., Wei, Y., Li, H., Wu, X., Xu, J., Tu, S., Zhang, Y., Chen, H., & Cao, B. (2020). Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. *Lancet*, *395*, 1054–1062. https://doi.org/10.1016/S0140-6736(20)30566-3

How to cite this article: Saad, H. M., GamalEl Din, S. F., Elbokl, O. M., & Adel, A. (2022). Predictive factors of erectile dysfunction in Egyptian individuals after contracting COVID-19: A prospective case–control study. *Andrologia*, 54, e14308. https://doi.org/10.1111/and.14308