



# Erectile dysfunction among Thai patients with COVID-19 infection

Kawintharat Harirugsakul<sup>1^</sup>, Sorawit Wainipitapong<sup>2^</sup>, Jeerath Phannajit<sup>3</sup>, Leilani Paitoonpong<sup>4</sup>, Kavirach Tantiwongse<sup>1^</sup>

<sup>1</sup>Division of Urology, Department of Surgery, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, the Thai Red Cross Society, Bangkok, Thailand; <sup>2</sup>Department of Psychiatry and Center of Excellence in Transgender Health (CETH), Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, the Thai Red Cross Society, Bangkok, Thailand; <sup>3</sup>Division of Clinical Epidemiology and Division of Nephrology, Department of Medicine, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, the Thai Red Cross Society, Bangkok, Thailand; <sup>4</sup>Division of Infectious Diseases, Department of Medicine, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, the Thai Red Cross Society, Bangkok, Thailand

*Contributions:* (I) Conception and design: K Harirugsakul, S Wainipitapong, K Tantiwongse; (II) Administrative support: K Tantiwongse; (III) Provision of study materials or patients: L Paitoonpong; (IV) Collection and assembly of data: K Harirugsakul; (V) Data analysis and interpretation: K Harirugsakul, S Wainipitapong, J Phannajit; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

*Correspondence to:* Kavirach Tantiwongse. Division of Urology, Department of Surgery, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, the Thai Red Cross Society, 1873, Rama IV Rd. Pathumwan, Bangkok, 10330, Thailand. Email: Kavirach@chula.md.

**Background:** Erectile dysfunction (ED) is suspected to be the symptom manifestation of COVID-19. However, scarce data was presented this day. Our study was conducted to determine the prevalence of ED and its associated factors among Thai patients with COVID-19.

**Methods:** Sexually active males with COVID-19, hospitalized between May and July 2021 at one university hospital in Bangkok, were screened for erectile dysfunction by the International Index of Erectile Function 5 (IIEF-5). Demographic data and COVID-19 treatment history were collected. Mental health status, including depression and anxiety, was evaluated with the Thai Patient Health Questionnaire 9 (PHQ-9) and the Generalized Anxiety Disorder Scale (GAD-7), respectively. The sample size was calculated, and logistic regression was used to analyze the association.

**Results:** One hundred fifty-three men with COVID-19 were recruited. ED prevalence was 64.7%, of which severity was mostly mild. Logistic regression, adjusted for age, BMI, and medical comorbidities, portrayed a significant association between ED and mental health status. Higher risk of ED was found in participants with major depression [adjusted OR 8.45, 95% CI: 1.01–70.96, P=0.049] and higher GAD-7 total score [adjusted OR 1.15, 95% CI: 1.01–1.31, P=0.039].

**Conclusions:** Thai patients with COVID-19 had high prevalence of ED, which was associated with mental disorders. Thus, screening for mental problems is recommended in individuals with COVID-19 and ED.

**Keywords:** Anxiety; COVID-19; depression; erectile dysfunction (ED)

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<sup>^</sup> ORCID: Kawintharat Harirugsakul, 0000-0002-8332-1242; Sorawit Wainipitapong, 0000-0001-6306-0930; Kavirach Tantiwongse, 0000-0001-8557-924X.

## Introduction

The global COVID-19 pandemic, caused by the SARS-CoV-2 virus, has affected entire populations worldwide. Apart from the respiratory system, which is its main manifestation, extrapulmonary manifestations of COVID-19 infection could also be found, including symptoms of the reproductive system. The negative impact on male reproductive health should be of concern because the virus can directly injure testicular tissues by binding with angiotensin-converting enzyme 2 (ACE2) receptors highly expressed in the reproductive organs (1). The presence of virus in penile tissues, and relatively lower levels of endothelial progenitor cells were reported in two patients with a history of COVID-19 infection. They were subsequently diagnosed with severe erectile dysfunction (ED) which could be explained by endothelial dysfunction (2).

In patients with COVID-19, ED is caused by multiple physical and mental etiologies such as endothelial dysfunction, subclinical hypogonadism, pulmonary hemodynamic impairment, and mental comorbidities (3). Mental health problems are considered to be an obvious consequence of the pandemic. Higher rates of psychiatric disorders were globally reported during the outbreak, including major depression and anxiety disorders (4). These several contributing factors complicate the etiologies of ED in the pandemic among men in good health and male patients with either recovered or current COVID-19 infection.

Although patients with current COVID-19 infection should have the highest risks of developing ED, studies in this population are limited. Twenty-five COVID-19 positive patients were reported to have higher ED prevalence than seventy-five participants from the control group (5). Furthermore, population-specific studies are necessary for sexual dysfunction research because of region-specific cultural differences and conservative beliefs, especially in Asian countries, where sexual dysfunctions are usually undiagnosed and untreated (6).

To date, there is still no study evaluating ED and its contributing factors among patients with COVID-19 infection in Thailand. It is questionable whether ED in this Asian country would differ from previous studies in non-Asian populations. The aim of our study was to measure the prevalence of ED by using a Thai version of the International Index of Erectile Function 5 (IIEF-5) among patients with current COVID-19 infection. We also examined the correlation between ED and related factors,

including age, BMI, mental health status and COVID-19 treatment during hospitalization.

We present the following article in accordance with the STROBE reporting checklist (available at <https://dx.doi.org/10.21037/tau-21-807>).

## Methods

### *Study population*

Between May and July 2021, all sexually active males, defined as self-reported having sexual intercourse in recent two weeks, patients aged between 18–70 years old who were hospitalized for COVID-19 infection at one university hospital in Bangkok, Thailand, were invited for assessment. Those with severe medical and mental illnesses were excluded. Prior to assessment, informed consent was obtained verbally or via an online application for prevention of viral transmission. Instead of online assessment questionnaires, phone interview was done with participants who were illiterate. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by Chulalongkorn University's Institutional Review Board (IRB No. 408/2021) and informed consent was taken from all the participants.

Demographic data including age, BMI, underlying diseases, and history of alcohol and nicotine use were obtained. Details about COVID-19 vaccination and treatment during hospitalization were extracted. The sample size was calculated based on prior studies and required a total sample of seventy-eight (5).

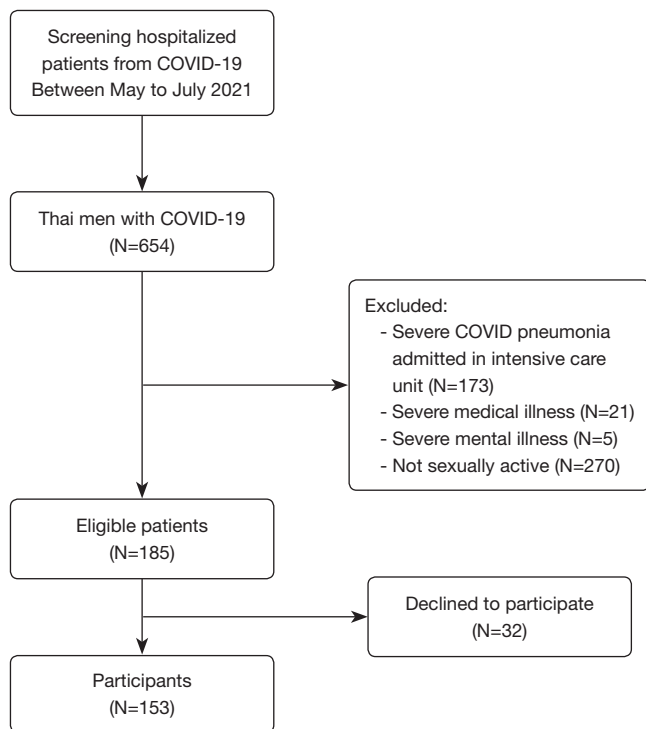
### *A Thai version of the International Index of Erectile Function 5 (IIEF-5)*

Erectile function was measured by a Thai version of IIEF-5. This tool has five questions focusing on ED and satisfaction of sexual intercourse. Its scores negatively correlated with ED severity and could be classified into five levels; severe [5–7], moderate [8–11], mild to moderate [12–16], mild [17–21], and no ED [22–25] (7).

### *Mental health status*

#### **The Thai Patient Health Questionnaire 9 (PHQ-9)**

The PHQ-9 was used to evaluate depressive symptoms, including depressed mood, loss of interest and energy, sleep and appetite problems, feelings of worthlessness, trouble



**Figure 1** Study protocol.

concentrating, psychomotor abnormalities, and thoughts of death or self-injury. A PHQ-9 score of  $\geq 9$  is considered positive for major depression, with sensitivity and specificity of 0.84 and 0.77 respectively (8).

### The Generalized Anxiety Disorder Scale (GAD-7)

The GAD-7 scale is an assessment for generalized anxiety disorder and anxiety severity. The measured symptoms included nervousness, uncontrolled and excessive worrying, trouble relaxing, restlessness, irritability, and fear that something awful might happen. A GAD-7 score of  $\geq 10$  represents a cut point for identifying generalized anxiety disorder with sensitivity and specificity of 0.89 and 0.82, respectively (9).

### Statistical analysis

Descriptive statistics were used to report demographic data, mental health status and COVID 19 treatment. Categorical variables were presented as counts and percentage, and continuous variables were shown in mean with SD or median with interquartile range (IQR) as appropriate. We used Pearson's Chi-square or Fisher's exact test to determine

the difference among categorical data and student *t*-test or Mann-Whitney U test for continuous data. Bivariate and multivariable logistic regression were used to explore factors associated with erectile dysfunction. For multivariable model, we planned to adjust clinically important covariates including theoretically associating factor of ED together with factor with P value below 0.20 in bivariate model. A P value of  $<0.05$  was considered statistically significant. STATA-IC Version 16.1 was used for analyzing data.

### Results

Throughout the study period, 654 Thai men with COVID-19 were screened. We excluded 469 patients according to the criteria. Of the rest, 32 patients refused to participate, so the remaining 153 sexually active men were enrolled in our study (Figure 1). Mean age and BMI was 40.8 years and 25.6 kg/m<sup>2</sup>, respectively. Most were married or couple (81.7%), employed (93.5%), and had educational attainment lower than bachelor's degree (84.3%). In all participants, morning erection tended to be normal. Only 32.7% of the participants received COVID-19 vaccination, and 8 participants reported having sex with male partners. Previous use of ED medications was reported in 6 participants. There were 8 and 21 participants who screened positive for generalized anxiety disorder and major depression respectively. The overall prevalence of ED was 64.7%. Mild ED (45.1%) was the most prevalent, followed by moderate (15.7%), and mild to moderate (3.9%) severity. None of the participants had severe ED. Numbers of underlying diseases, past history, and substance use are shown in Table 1.

The details of COVID-19 treatment during hospitalization were shown in Table 2. Most participants were symptomatic (92.8%) or mild symptoms and received supportive treatment (93.5%). Corticosteroids was given to 36 participants. Meanwhile, favipiravir was prescribed seven times more than remdesivir and fourteen times more than tocilizumab. The use of each medication depended on increasing severity of COVID-19. Oxygen supplement via nasal oxygen cannula was provided for 20 participants. Regarding the severity of respiratory difficulties, 1 and 4 received an additional helmet noninvasive ventilation and high-flow nasal oxygen cannula, respectively.

Multivariable logistic regression was done (Table 3). We found a significant association between having ED and mental health status after correcting for age above forty

**Table 1** Demographic characteristics, mental health, and erectile function measurement

Participants (N=153)	ED (N=99)	Non-ED (N=54)	P value
Age (mean ± SD)	41.3±10.8	39.7±11.1	0.37
Body mass index (mean ± SD)	25.9±4.5	25.6±4.4	0.28
Marital status, n (%)			0.39
Single	15 (15.2)	10 (18.5)	
Married or couple	81 (81.8)	44 (81.5)	
Separated or divorced	3 (3.0)	0 (0.0)	
Educational status, n (%)			0.35
Lower than bachelor's degree	81 (81.8)	48 (88.9)	
Bachelor's degree or upper	18 (18.2)	6 (11.1)	
Medical comorbidities	19 (19.2)	10 (18.5)	0.92
Diabetes Mellitus	9 (9.1)	4 (7.4)	0.72
Hypertension	8 (8.1)	8 (14.8)	0.19
Hypercholesterolemia	8 (8.1)	3 (5.6)	0.56
Substance use, n (%)			
Active alcohol drinking	14 (14.1)	12 (22.2)	0.2
Active smoking	38 (38.4)	19 (35.2)	0.7
Mental health status			
GAD-7 total score [median (IQR)]	4 [1–7]	2 [0–3]	0.004*
Anxiety disorder (GAD-7 ≥10), n (%)	8 (8.1)	0 (0)	0.032*
PHQ-9 total score [median (IQR)]	3 [1–8]	2 [0–4]	0.015*
Major depression (PHQ-9 ≥9), n (%)	20 (20.2)	1 (1.9%)	0.002*
Normal morning erection, n (%)	84 (84.8)	45 (83.3)	0.81
COVID-19 vaccination, n (%)	33 (33.3)	17 (31.5)	0.82

\*, P value <0.05. ED, erectile dysfunction; GAD-7, Generalized Anxiety Disorder Scale; PHQ-9, Patient Health Questionnaire 9; SD, standard deviation; IQR, interquartile range.

years which is the main age range affected by ED (10), BMI of more than 23 kg/m<sup>2</sup> which determined overweight in Asian population (11), and medical comorbidities including

**Table 2** COVID-19 treatment during hospitalization

Variables	Total, N (%)	ED, N (%)	Non-ED, N (%)	P value
COVID-19 diagnosis				0.17
Pneumonia	63 (41.2)	44 (69.8)	19 (31.2)	
Pharyngitis	79 (51.6)	46 (58.2)	33 (40.8)	
Asymptomatic	11 (7.2)	9 (81.8)	2 (18.2)	
Medications				
Favipiravir	70 (45.8)	48 (68.5)	22 (31.5)	0.36
Corticosteroids	36 (23.5)	24 (66.7)	12 (33.3)	0.78
Remdesivir	10 (6.5)	9 (90.0)	1 (10.0)	0.08
Tocilizumab	5 (3.3)	4 (80.0)	1 (20.0)	0.47
Oxygen supplement	20 (13.1)	15 (75.0)	5 (25.0)	0.3

ED, erectile dysfunction.

hypertension, diabetes mellitus and hypercholesterolemia. ED was more prevalent in participants whose PHQ-9 total score indicated major depression [adjusted OR 8.45, 95% CI: 1.01–70.96, P=0.049], and those with higher GAD-7 total score [adjusted OR 1.15, 95% CI: 1.01–1.31, P=0.039]. However, a statistically significant association was not seen among other variables.

### Discussion

ED, the most concerning male sexual dysfunction (12), has not been widely studied in Thailand and some Asian countries. Even in this pandemic, several studies have focused on the impact of COVID-19 upon multiple dimensions of health but not on sexual function. The exact prevalence of ED among the Thai population is still lacking, both in general situations and during the COVID-19 pandemic.

The prevalence of ED among Thai patients with COVID-19 was 64.7%. This was significantly higher than findings from previous studies (13,14) in the normal Thai population, which estimated the prevalence around 37.5–42.2% (two proportion Z-test P<0.05). One study from Italy also reported higher prevalence of ED in COVID-19 groups compared to the normal population, after adjusting for age, BMI and psychological status (5). However, the prevalence of ED in COVID-19 patients in Thailand was significantly higher than in Italy (64.7% vs. 28%, P<0.05).

**Table 3** Bivariate and multivariable logistic regression between ED and associated factors

Variables	Bivariate analysis		Multivariable analysis	
	Crude OR [95% CI]	P value	Adjusted OR [95% CI]	P value
Age	1.01 [0.98, 1.05]	0.37		
Age above 40 years	1.57 [0.81, 3.07]	0.18	2.08 [0.93, 4.65]	0.075
BMI	1.04 [0.97, 1.03]	0.28		
Overweight (BMI $\geq$ 23 kg/m <sup>2</sup> )	0.89 [0.42, 1.88]	0.76	0.67 [0.29, 1.53]	0.34
Married or couple	1.02 [0.43, 2.41]	0.96		
Active smoking	1.15 [0.58, 2.29]	0.7		
Active alcohol drinking	0.58 [0.25, 1.36]	0.21		
Medical comorbidities (including HTN, DM, HCL)	1.05 [0.45, 2.44]	0.92	0.54 [0.20, 1.52]	0.245
GAD-7 total score	1.21 [1.08, 1.37]	0.002*		
Anxiety disorder (GAD-7 $\geq$ 10)	1.00 [-]	–	1.15 [1.01, 1.31]	0.039*
PHQ-9 total score	1.15 [1.04, 1.28]	0.01*		
Major depression (PHQ-9 $\geq$ 9)	13.42 [1.75, 103.01]	0.01*	8.45 [1.01, 70.96]	0.049*
Normal morning erection	1.12 [0.45, 2.76]	0.81		
COVID19 vaccination	1.09 [0.53, 2.21]	0.82		
COVID19 pneumonia	1.47 [0.74, 2.92]	0.27		

\*, P value <0.05. HTN, hypertension; DM, diabetes mellitus; HCL, hypercholesterolemia; GAD-7, Generalized Anxiety Disorder Scale; PHQ-9, Patient Health Questionnaire 9.

We believed our differing results might be determined by both medical and psychological factors.

The differences of ACE2 receptors could genetically explain the variation in susceptibility to SARS-CoV-2 infection. The ACE2 gene polymorphism alters the number of ACE2 receptor expression, which is a binding site of the SARS-CoV-2 virus. Higher ACE2 expression is more frequent in some regions of Asia, including Thailand, and is associated with increased viral susceptibility. This genetic difference may account for the higher ED prevalence in Thailand (15).

The variants of SARS-CoV-2 are also responsible for the severity and infectivity of COVID-19 (16). Our study was done during mid-2021 which was the peak period of the B.1.1.7 variant spreading in Thailand. Well known in high transmission rate and increased severity, this strain might be dissimilar to the variant, which was not mentioned, from previous study (17,18).

Our participants' mean age was older than the study in Italy, with a maximum reaching sixty-five years, and mean BMI was also higher (25.6 *vs.* 22.5 kg/m<sup>2</sup>). This may be another factor, among several related bio-psychological

factors that should be considered as an explanation for the difference in ED prevalence.

Interestingly, age, BMI and medical comorbidities understood to be ED risk factors were not significantly associated with ED. This could be explained by the low number of our sample size. Most participants reported having a normal morning erection, which might indicate an intact erection capacity. Thus, these biological factors might play less part in ED etiologies among our participants. Psychological impacts, including stress, anxiety, and depression, should be emphasized since they were highly correlated with ED during this pandemic, found in the prior study (19).

Mental health status was found to have remarkable influence. We used a PHQ-9 cut-off score of  $\geq$ 9 to classify patients as having depression, according to the validated cut-off in the Thai population. Unfortunately, the GAD-7 has never been validated in Thailand, so we used its total score instead.

Bivariate logistic regression showed significant association between ED and these two variables; PHQ-9  $\geq$ 9 (P=0.01) and GAD-7 total score (P=0.002). Multivariable

logistic regression, adjusted for age, BMI, and medical comorbidities, also confirmed our result.

Psychogenic causes should be a primary focus for ED younger men (20). Psychological burdens, including anxiety, depression, and poor socioeconomic status, are significant risk factors of developing ED (21). During the COVID-19 pandemic, unemployment and financial crisis affected a large proportion of the Thai population, and were associated with adverse mental health outcomes (22,23). Considering the current economic crisis in Thailand and its impact upon mental health, psychological issues may also contribute to the higher ED prevalence in our study population. In addition to ED, sexual dissatisfaction was also increased during this pandemic situation (24).

Compared to patients hospitalized for non-COVID-19 conditions, the number of participants with major depression in our study was comparable; meanwhile, the prevalence of generalized anxiety disorder was lower (25,26). However, the prevalence of mental problems among hospitalized patients was varied regarding each disease severity or its impact on quality of life. The study about ED prevalence during hospitalization was lacking. Many previous studies reported the number of ED in patients with stable and chronic diseases, which depended on different diagnoses (38.6–82%) (27–31).

Compared to prior ED and COVID-19 studies, our study covered a larger sample size. All participants were confirmed with SARS-CoV-2 RT-PCR and diverse in severity and treatment. We collected important ED-related factors, including medical comorbidities, substance abuse, and mental health status.

Some limitations should be discussed in this study. It was designed in a cross-sectional method, therefore the causal relationship between ED and associated factors could not be explored. Our study population is comprised of inpatients, leading to limited generalizability to patients with mild COVID-19 who do not require hospitalization. Furthermore, investigations such as hormonal level, nocturnal penile tumescence testing, or duplex doppler ultrasound could not be conducted due to risk of COVID-19 transmission. All questionnaires could also be influenced by recall bias; thus the responders might reply mainly based on their recent periods (32). However, it was beneficial in terms of the results that could better represent the status of each individual during his acute illness of COVID-19 infection. Future prospective studies will be useful for identifying the causation of ED or its long-term effects caused by COVID-19. Also, further studies focusing

the management and its accessibility are still needed to alleviate the impact of COVID-19 on men's health (33).

## Conclusions

The prevalence of ED among Thai patients with COVID-19 was high. ED should be assessed as multifactorial in origin, with consideration for psychological factors. Healthcare providers are suggested to screen for mental problems in individuals with ED and vice versa, with prudent cultural consideration.

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## Footnote

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