

REVIEW ARTICLE



Erectile dysfunction among patients and health care providers during COVID-19 pandemic: A systematic review

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COVID-19 pandemic is associated with devastating effects on social, psychological, and economical aspects of survivors. We assume that erectile function (EF) is affected as well. We performed a systematic review of the published articles about the change in EF among patients and health care providers during the COVID-19 pandemic. We searched PubMed and Cochrane databases for English literature using a combination of medical subject headings (MeSH) terms and keywords. We extracted data of erectile dysfunction (ED) rate, international index of erectile function (IIEF), changes related to exposure to the pandemic (Primary objectives), and factors affecting these differences (Secondary objectives). Twenty articles were included in the screening phase. Only 3 articles were eligible for primary objectives, and 2 articles were included for the secondary objective. Three articles revealed an increase in ED cases and a reduction in IIEF-5 scores during the pandemic. Rates of ED have ranged from 32% to 87% of the study populations. Anxiety, depression, and post-traumatic stress disorder (PTSD) were associated with increased ED rates. We conclude that the COVID-19 pandemic is associated with increased rates of ED. Anxiety and depression augment this increase. Health care providers are at higher risk for PTSD, which increases the risk of ED.

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INTRODUCTION

In 2020, World Health Organization declared COVID-19 as a pandemic [1]. Since then, the number of affected individuals was globally increasing [2]. Mortality rates were also increased to numbers that were not previously accustomed since the Spanish flu and World Wars [2, 3]. Numbers were publicly announced on daily basis. Health care systems were markedly burdened [4], and many countries have suffered from severe deficiencies in medical supplies [5]. Accordingly, all countries have obligated their people to follow lockdown policies to prevent further spread, and many families were further loaded at economic and social levels.

Several reports showed that sexual function was affected during and after the pandemic [6–10]. The number of diagnosed cases with sexual dysfunction was increased among males [11] and females [12, 13]. Men's complaints have included decreased libido and orgasm [14], erectile dysfunction (ED) [6], and decreased sexual satisfaction in comparison to a pre-COVID state [15]. Of note that many patients have reported a decrease in erectile function (EF), which was confirmed by a reduction of their international index of erectile function (IIEF) assessment [16].

The high incidence of sexual dysfunction during the pandemic was the interest of several studies that tried to address the underlying etiology. Assumptions of biological underlying mechanisms such as hypogonadism, endothelial and cardiopulmonary dysfunction were proposed [17]. On the other hand, several other studies have shown that psychological disturbances, e.g., anxiety or depression, were the principal underlying etiology of sexual dysfunction during the pandemic [7, 15, 16].

This article has reviewed the status of EF among patients and health care providers during the COVID-19 pandemic. Further, it has addressed the social and economic effects of lockdown as proposed risk factors for ED.

The rationale of the current study was to demonstrate whether a realistic association would be present between the COVID-19 pandemic and ED and to identify the factors that may affect changes in EF during the pandemic. This study highlighted the need for more prospective research to identify the possible underlying etiology of ED during the COVID-19 pandemic.

MATERIALS AND METHODS (EVIDENCE ACQUISITION)

The methodology was designed before the revision of articles and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [18]. The protocol was registered in the PROSPERO registry by the number (CRD42021248283).

Literature search methodology

PubMed and Cochrane's databases were searched for English articles published from 1/1/2020 to 6/2/2021. The language was restricted to facilitate the revision of full articles. We used combined medical subject headings (MeSH) terms and keywords to build a search strategy. MeSH terms included; COVID-19, SARS-COV-2, COVID-19 post-intensive care syndrome, post-acute COVID-19 syndrome, erectile dysfunction, and penile erection. Keywords included erectile function, SARS, sexual dysfunction, and impotence. Reference lists were reviewed for related articles.

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Study selection

Articles were reviewed independently by the authors (AB and AE). Disagreement was solved by discussion. The target articles were any full article of cross-sectional design, that investigated the status of EF during the pandemic, either quantitatively or qualitatively. The targeted population was adult males (>18 years old), regardless of marital status. Study groups included health care workers, COVID-19 survivors, and persons locked down due to the pandemic. Comparison groups have no or less exposure to these risks factors than the study groups. The outcome were assessed in terms of subjective ED complain and further IIEF-5 score [19].

Data extraction

Data were extracted by the two authors (AB and AE). Data has included: title, author, journal name, date of publishing, and the state of lockdown in the authors' country at the time of data collection. Participant's data has included sample size, average age, whether females are included in the study for other purposes, and the number of positive cases with diagnosis of COVID-19. Outcome data have included the rate of ED, an average IIEF-5 score, and the significance of the difference in study groups. Data of risk factors have included correlation with being a health care provider, marriage status, alcohol consumption, previous history of sexual dysfunction, and rate of sexually transmitted disease. Data about the frequency of sexual life and the significance of association were also gathered.

Data synthesis and analysis

This systematic review has investigated the change in EF during and after the COVID-19 pandemic (primary objective). The secondary objective was to screen the risk factors that were associated with changes in EF during the pandemic and its consequences. Due to the obvious heterogeneity among the inclusion criteria, study and control populations, methodologies, and measures of effect estimates, the synthesis of meta-analysis and forest plots were not applicable.

On the other hand, techniques of synthesis without metanalysis were implemented [20]. *P*-values of changes in ED status were combined using Fisher's method [21]. Sensitivity analysis of *p*-values combination was done restricted by the type of measurement used to indicate ED status; IIEF-5 score versus percent of patients with ED. Prevalence of ED during the pandemic was reported using percentage. Median and range were used to summarize the distribution of prevalence data. We draw a bubble plot to visualize the relation between the prevalence of ED and sample size.

The approval of the Institution Review Board is not applicable in this review.

RESULTS (EVIDENCE SYNTHESIS)

Literature search

The systematic search of PubMed and Cochrane Reviews databases returned 20 records. Cochrane search returned 4 articles: 1 Cochrane review, and 3 reports from the ClinicalTrials.gov registry. There were no duplicates. Seventeen articles were excluded after revising the title and abstract. Excluded articles were reviews [17, 22], perspectives [23, 24], a letter [25], case reports [8, 14], studies about the treatment of COVID-19-related disease other than ED [26–28], articles considering female sexual dysfunction only [12, 13, 29], and all 4 records from Cochrane search. Three articles were included in the full qualitative synthesis process [6, 11, 16]. However, 2 articles [7, 15] had no eligible comparison groups, and they were included for the secondary objectives only (prevalence of ED, and investigation of risk factors). PRISMA diagram is shown in (Fig. 1).

Study characteristics

Table 1 shows the characteristics of the included studies. They included health care providers [6, 7], patients who have presented to the andrology clinic during the pandemic [11], and persons who have responded to online questionnaires during and after lockdown periods [15, 16].

Primary outcomes were sexual dysfunction [6, 11], decrease in EF and ejaculatory control [16], sexual satisfaction [15], and sexual attitude [7]. The study-design was non-randomized in all studies. Three studies had compared to male groups [6, 11, 16], one had compared to female group [15], and one study was non-comparative [7]. Except in one study [16], data were collected during the period of the local COVID-19 breakout, and most populations were locked down.

Participants attending the andrology clinic [3] were older than health care workers [6, 7] and social media users [16]. The control group was older than the study group in one study only [11].

Outcome measures

Change in EF. To measure the changes in EF, the IIEF-5 score was used in 2 studies [6, 16]. Change in percentage of patients with ED was used in one article [11] (Table 2).

In 2 studies, authors have compared EF status in participants during the COVID-19 pandemic with status before the pandemic [11, 16]. In the third [6], the authors have compared health care providers dealing with suspected and confirmed COVID-19 cases with patients attending the urology clinic during the pandemic.

All articles have reported a reduction in EF in association with exposure to the COVID-19 pandemic. There was significant reduction in mean IIEF-5 score ($p < 0.001$) [16], and significant increase in patients with ED after pandemic ($p < 0.008$) [11]. Health care providers had a higher rate of ED ($p < 0.001$), and lower median IIEF-5 scores than non-healthcare workers ($p < 0.001$) [6].

The heterogeneity among populations of the included studies prevented us from the quantitative synthesis of data. However, the *p*-values can be combined from two studies [20, 21]. For analytical purposes, we considered the reported *p*-values by Bulut et al., as if it has 2 investigations: the first for the change in median IIEF, and the second for the change in the rate of ED. The combined *p*-value for the 4 comparisons was ($p < 0.00001$, $\text{Chi}^2 = 56.6$, degrees of freedom = 8). Considering sensitivity analysis, studies that reported changes in IIEF-5 [6, 16] have revealed no change in combined *p*-value ($p < 0.00001$, $\text{Chi}^2 = 26.2$, degrees of freedom = 4). When considering studies that have reported changes in ED rates [6, 11], the combined *p*-value was ($p < 0.00001$, $\text{Chi}^2 = 30.4$, degrees of freedom = 4).

There was strong evidence supported that EF status and scores were negatively affected by exposure to the COVID-19 pandemic. There was an increase in number of ED patients and a reduction in IIEF-5 scores during the pandemic in comparison to before the pandemic. The same results were reported among health care providers when compared to patients attending urology clinics.

Assessment of ED. Most studies used a scoring system to assess ED. Three studies considered specific cut-off points of IIEF-5 scores <21 [6, 15], or IIEF score <25 [7]. Two studies defined ED as any decrease in the IIEF-5 score [16], or as a clinical-based diagnosis [11] (Fig. 2).

Accordingly, the rate of ED among populations who responded to online questionnaires was 32% [15, 16]. The rate of ED was higher among health care providers 40% [7] and 82% [6]. The highest rate (87%) was reported among older men attending andrology clinics during the pandemic [11].

Meta-analysis cannot be achieved due to clear differences among population characteristics. Data are summarized into a bubble plot (Fig. 3). The median value detected during the pandemic was 40%, and range from 32% to 87%.

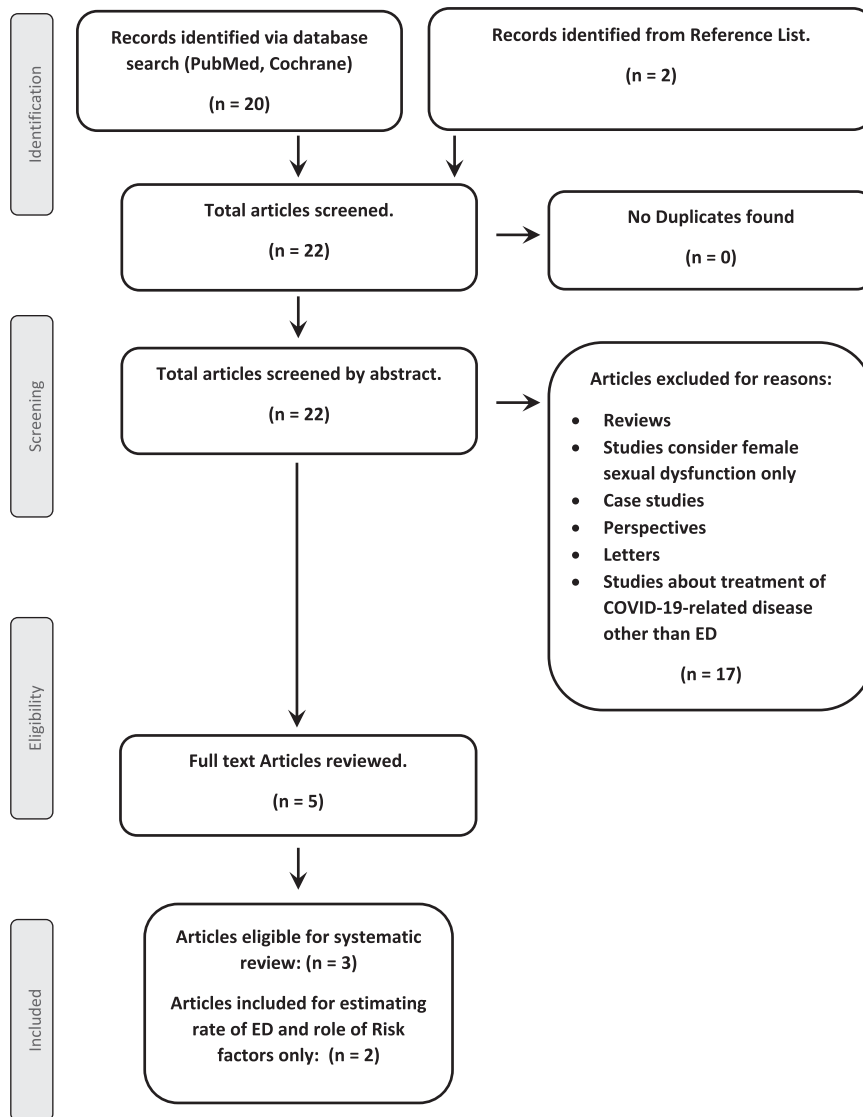


Fig. 1 PRISMA data flow diagram for systemic search of databases. Twenty articles were identified from database search, while five articles were included into systemic review.

Risk factors associated with EF changes. All studies have agreed that increased anxiety scores (Generalized Anxiety Disorder-7 (GAD-7) questionnaire, or State-Trait Anxiety Inventory-1 (STAI-I)) were associated with increased rates of ED [7]. Post-traumatic stress disorder (PTSD) score (Impact of Event Scale-Revised (IES-R)) was increased among health care providers and was associated with the increase in ED rates [6]. Increased depression score (Patient Health Questionnaire-9 (PHQ-9)) was also associated with increased ED [15, 16], however, there was no association with Beck score [7]. Reduced frequency of sexual life and dissatisfaction was associated with more prevalence or severity of ED [15, 16] (Table 3).

The rate of ED was not affected by age, marital status, educational level, history of sexual dysfunction or intake of related drugs, smoking, chronic diseases, income level, occupational or economic changes. The association between increased ED rates and alcohol consumption was controversial. Being a health care provider or working in proximity to confirmed COVID-19 cases showed insignificant association with the increased rate of ED in 2 studies.

Frequency of sexual life. Reduction in frequency of sexual practice was associated with an increase in ED rate [16]. Changes in sexual

life frequency after the pandemic was not universal. There was a significant reduction in the frequency of sexual practice per week among health care providers (1.32 (± 1.27) during COVID-19 pandemic, vs 2.53 (± 1.12) before pandemic; $p < 0.001$) [7], while the number per month was not changed among social media users (5.42 (± 6.4) after pandemic vs 5.32 (± 5.73) before pandemic; $p = 0.713$) [16].

DISCUSSION

EF is always influenced by psychological as well as physiologic status and interaction of therapy for different concomitant conditions [30, 31]. Individuals who survived the COVID-19 pandemic were exposed to stressful events in terms of social, economic, and health issues. In the post-COVID-19 era, concerns were raised regarding possible long-term consequences. The pathogenesis of COVID-19 is not yet well understood, and investigation of the possible complications becomes mandatory.

Reviewing a rapidly evolving literature of COVID-19 offered few studies that investigated ED and sexual dysfunction among men. After more than one year of the initial spread of COVID-19, only 5 articles have addressed the rate of ED among survivors.

Table 1. Methodologic and demographic characteristics of 5 studies included in the review.

Study	Bulut et al.	Duran et al.	Omar et al.	Fang et al.	Culha et al.
Country	Turkey	Turkey	Egypt	China	Turkey
Study group	Health care professionals	Patients present to andrology clinic during pandemic	Male social media users	Male social media users after pandemic	Health care professionals during pandemic
Comparison group	patients attending Urology clinic	Patients presented to andrology clinic before pandemic	Female social media users	Male social media users before pandemic	Health care professionals before pandemic
Primary outcome	Sexual function	Sexual function	Sexual satisfaction	Deterioration of EF or ejaculation control	Sexual attitude
Demographic data					
Genders	Males	Males	Males & Females	Males	Males & Females
% of males	100%	100%	31%	100%	52%
Age, Study Group	NM	50.6 (17.1)	NM	NM	30.65 (5.99)
Mean (SD)	32 (Min:Max: 20–55)	NM	NM	28 (IQR: 24–35)	NM
Median					
Age, Comparison group	NM	55.3 (16.9)	NA	NM	NA
Mean (SD)	34 (Min/Max: 19–55)	NM	NA	28 (IQR: 24–35)	NA
Median					
Sig. of difference	0.7	<0.001	NA	NM	NA
Methodology					
Study Design	Comparative, non-randomized	Comparative, non-randomized	Comparative (with females) non-randomized	Comparative non-randomized	Non-comparative non-randomized
Study group (Nu)	159	1724	217	251	185
Control group (Nu)	200	3231	NA	251 (same patients)	NA
Date of data collection	Around May 2020	March 12 to June 1, 2020	March 30 to June 3, 2020	NM	2 to 26 May 2020
Local pandemic state during data collection	during the pandemic	during the pandemic	during the pandemic	NM	during the pandemic
Lockdown state during data collection	Weekend lockdown	Weekend lockdown	Night time lockdown	NM	Weekend lockdown
Nu. of COVID positive	NM	NM	22	3	NM

EF erectile function, IQR inter-quartile range, NA not applicable, NM not mentioned, Nu number, SD standard deviation.

On the other hand, patients attending clinics seeking advice about sexual health were increased, and diagnoses of sexual and other andrological diseases were also augmented during the pandemic [11].

There was an increase in rates of ED during and after the pandemic. There was also a significant reduction in IIEF-5 scores, which indicated an increase in the severity of ED. The significance of these changes was confirmed after combining p-values of the 3 studies that have investigated this issue (Table 2). In the current study, we have used sensitivity analysis to investigate the effect of heterogeneity among measures of effect estimates. We also combined p-values from studies that reported the change in the rate of ED and combined p-values from studies that reported the change in IIEF-5. Both tests agreed with our initial proposal.

The 5 studies have investigated the possible correlation between ED and psychological changes. Although psychological factors have played a critical role, biological and pathological factors cannot be excluded especially when the available data about the diagnosis of COVID-19 was limited. Furthermore, since infection can be asymptomatic in a significant number of patients,

Table 2. Significance of change in ED rates and IIEF-5 scores after COVID-19 pandemic.

Study	Bulut et al.	Duran et al.	Fang et al.
Measurement	IIEF-5	NM	IIEF-5
Study group			
Mean IIEF (SD)	NM	NM	17 (7.15)
Median IIEF (min-max)	13 (5–24)	NM	20(1–25)
ED rate	82.4%	87%	31.9%
Comparison group			
Mean IIEF (SD)	NM	NM	18.13 (6.74)
Median IIEF (min-max)	21 (7–25)	NM	21 (1–25)
ED rate	50.5%	66%	NM
Difference between groups			
Mean IIEF score, p-value	NA	NA	< 0.001
Median IIEF score, p-value	<0.001	NA	NM
Rate of ED, p-value	<0.001	0.008	NA

ED erectile dysfunction, IIEF International Index of Erectile Function, NM not mentioned, NA not applicable.

we cannot count psychological factors as the only underlying etiology of ED in the post-COVID-19 era.

The prevalence of ED during the pandemic ranged from 32% to 87%. Studies that have used social media to collect data have reported the lowest rate of ED [15, 16]. Those studies may have reflected the characteristics of social media users who may be younger in age. The study that have considered the older population during the pandemic have reported the highest prevalence [11]. The estimated prevalence of ED ranged from 40% to 82% in a special group of health care providers who were in close contact with COVID-19-positive patients.

The global prevalence of ED before the pandemic was variable. It was reported (3–76.5%) [32], (2–86%) [33], and (16.1%) [34], among patients with different ages. Studies from the Middle East area have reported the rate of ED to be 92.6% of patients visiting andrology clinics [35], 49.9% of adults older than 18 years [36], and 45.1% among internet users [37]. However, It was unfeasible to perform a precise comparison between absolute numbers among reports before and after the pandemic.

As expected, an increased ED rate is associated with decreased satisfaction during intercourse, and also with a reduced number of sexual practices. The fear of catching infection or infecting the partners play a role in amplifying the prevalence of anxiety and associated ED [6, 7]. Fears of transmitting an asymptomatic infection can contribute to increased anxiety and depression scores [7, 15, 16]. Furthermore, reduced physical contact during lockdown was associated with an increase in solitary sexual behaviors in the younger age group (18–32 yrs) [38]. Another study emphasized on the bidirectional relation between sexual activity and psychological status, and authors concluded that

Relation between size of study group per study and rate of ED

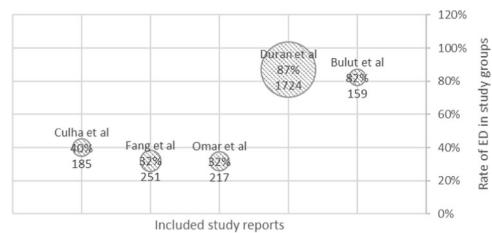
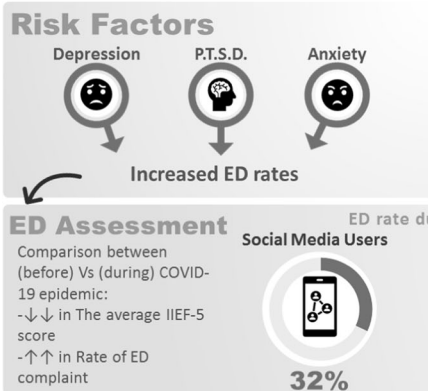


Fig. 3 A bubble plot of ED prevalence in study groups. The prevalence reported by each study presented in relation to the corresponding sample size.

Erectile Function Status in COVID-19 epidemic



Included Studies

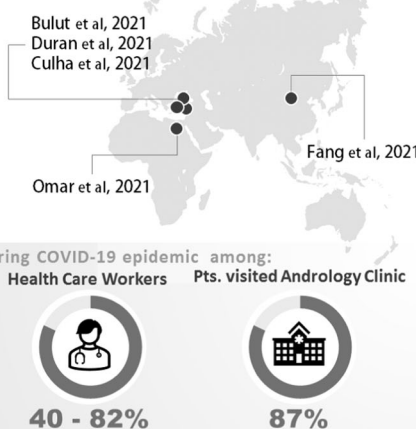


Fig. 2 Infographic of EF status in COVID-19 pandemic. Geographic distribution of included studies is shown (top right). Three risk factors were associated with changes in ED rates (top left). Changes occurred in EF parameters and rates of ED during pandemic are presented (bottom).

Table 3. Relation between potential risk factors and changes in ED rates after COVID-19 pandemic.

Study	Significant association (p -value < 0.05)		Insignificant association (p -value > 0.05)	
	Risk factor	Tool	Risk factor	Tool
Bulut et al.	PTSD	IES-R	Age	
	Health care provider		Marriage	
	Being a nurse more than a doctor			
	Proximity to confirmed cases.			
Omar et al.	Anxiety	GAD-7	None	
	Depression	PHQ-9		
	Sexual satisfaction	ISS		
Fang et al.	Anxiety	GAD-7	Health care provider	
	Depression	PHQ-9	Marriage	
	Reduced frequency of sexual life		Alcohol consumption	
			History of sexual dysfunction	
			Education levels	
			Smoking	
			History of erectogenic drug intake	
			Occupational changes	
			Economic changes	
Culha et al.	Anxiety	STAI-I	Anxiety score	STAI-II
	Alcohol consumption		Depression score	BECK
			Age	
			Proximity to confirmed cases.	
			Marriage	
			Education levels	
			Income level	
			Smoking	
			Chronic disease	

PTSD post-traumatic stress disorder, IES-R The Impact of Event Scale-Revised, GAD-7 Generalized Anxiety Disorder-7, PHQ-9 Patient Health Questionnaire-9, ISS Index of Sexual Satisfaction, STAI State-Trait Anxiety Inventory, BECK Beck depression inventory.

sexually active men who live with their partners during the pandemic have lower scores of GAD-7 and PHQ-9 [39]

No significant difference in age, marital status, education level, income level, chronic disease, and smoking rates between those who developed ED or showed a decrease in EF scores, and those who do not [6, 7, 16]. History of sexual dysfunction before the pandemic, either treated or not, was not associated with changes in ED rate after the pandemic [16]. Increased ED rates after the COVID-19 pandemic seem to be a special entity, not an exacerbation of a chronic condition.

There were controversial findings regarding the association of alcohol intake and increased ED [7, 16]. Although health care providers were facing higher levels of anxiety, an increase in ED among them was not reproducible [6, 16]. A recent study had addressed the considerations that should be put in mind during the assessment and treatment of ED patients. In that study, factors related to patient, partner, and physician judgment, all determine the course of ED and the response to the management plan. Among many important factors, patients and partner expectations, interrelation with the partner, satisfaction, and social factors are all affecting the EF status and the related therapeutic regimens [40].

The current study is limited by the availability of safe methods of interviewing patients during the pandemic. Authors in several studies relied upon social media to recruit cases, which might be biased toward special age groups. On the other hand, patients who had attended health care services during lockdown were not representing the general population, but a specific group of patients who were seeking urgent medical services. Further, Fisher's method

of combining p -values cannot address the magnitude of change. It assumes that the contribution of each study into the final p -value is equal to each other, and we could not estimate the weight of each sample size. Using median and range to summarize data about the prevalence of ED has not definitely addressed the effect of sample size in each study.

CONCLUSION

Exposure to the COVID-19 pandemic and its consequences was associated with increased anxiety, depression, PTSD, and sexual dissatisfaction. Both health care providers and the general population were affected but in variable degrees. Anxiety, depression, and PTSD were associated with an increase in ED cases and a reduction in EF score. This model emphasizes the effect of pandemic situation and similar disasters on the ability to maintain a normal sexual life.

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