Psychosexual health and sexuality: Multi-disciplinary considerations in clinical practice

Edited by

T. S. Sathyanarayana Rao and Henrique Pereira

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Psychosexual health and sexuality: Multi-disciplinary considerations in clinical practice

Topic editors

T. S. Sathyanarayana Rao — JSS Academy of Higher Education and Research, India Henrique Pereira — University of Beira Interior, Portugal

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*CORRESPONDENCE Henrique Pereira ☑ hpereira@ubi.pt

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Editorial: Psychosexual health and sexuality: multi-disciplinary considerations in clinical practice

Henrique Pereira (1) 1,2*

¹Department of Psychology and Education, Faculty of Social and Human Sciences, University of Beira Interior, Covilhã, Portugal, ²Research Centre in Sports Sciences, Health Sciences and Human Development (CIDESD), Vila Real, Portugal

KEYWORDS

psychosexual health, sex therapy, human sexuality, sexual minorities, COVID-19 pandemic on sexuality and sexual health

Editorial on the Research Topic

Psychosexual health and sexuality: multidisciplinary considerations in clinical practice

Human sexuality describes a global experience, framed in a given historical and sociocultural context of human evolution, which involves intimacy, social contact, procreation, sexual function, and sexual problems. The World Health Organization defines it as an integral human right, including sexual and reproductive rights and their respectful expression, not restricted to the absence of sexual problems. In this sense, the importance of considering the construct of psychosexual health is growing, integrating physical, psychological, and wellbeing aspects in the expression of people's sexuality, as well as openness to formal and systematized research sources, which will help to consolidate different contributions with applications to clinical practice. It is based on this premise that the creation of this thematic issue arose.

Resistance seems to persist when focusing on the study of human sexuality from a multidisciplinary perspective, with integration efforts of the different scientific contributions. This probably has to do with the need to optimize resources, but the truth is that there are countless intersections between psychological health and wellbeing and human sexual expression. An integrated view of human sexuality between psychology, biology, medicine, and sociology will help make this approach more visible and effective.

This Research Topic thus constitutes a tool to create a platform for sharing various contributions in a multidisciplinary way. Nine original articles, six quantitative articles, two systematic literature reviews, and a case report were received.

One such study (Buchholz et al.) aimed to assess the degree of correlation of prenatal androgen markers with online sexual compulsiveness and erectile function in young men, recruiting 4,370 participants. The results indicated that lower androgen levels were associated with higher levels of online sex compulsiveness, as well as a higher spermarche age correlated with higher levels of online sex compulsiveness. On the other hand, the more sexual compulsion, the lower the erectile function and ejaculatory control. These results allowed us to demonstrate the importance of intrauterine predisposition in mediating sexual behavior in adult men.

Another study (Hatta et al.) evaluated the psychosocial determinants of marital satisfaction among gynecological cancer survivors in 116 Malaysian patients. If, on the one hand, 37.9% of the participants said they had low levels of marital satisfaction, whereas

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psychosocial determinants (such as low education) were found to be associated with low marital satisfaction. Thus, this study demonstrated that sexual dysfunction and low levels of education can interfere with marital satisfaction among gynecological cancer survivors.

The third study included in this Research Topic assessed levels of quality of life and sexual health in an Indian city during the COVID-19 pandemic (Chatterjee et al.). In total, 1,376 individuals participated, of which 27.18% had sexual problems. From the point of view of emotional functioning, moderate levels of depression and anxiety were found, and older people and women showed greater worsening of sexual problems. This study contributed to demonstrate the importance of mental health in sexual functioning and quality of life.

The fourth contribution is the presentation of a case report whose purpose was to assess the challenges of transgender people in China (Shi et al.). The authors reinforce the idea that great progress has been seen in recent times and that they describe an important advancement in the protection of the rights of trans people, citing the example of people who go to the local police to request a new identity card after undergoing gender reassignment surgery. This mechanism represents a way of protecting the rights of trans people in China, allowing the transition to experience dignified gender expression, which also increases the visibility of the trans community and helps in the fight against transphobia in the country.

Another study (Cai et al.) evaluated the mental health of children with sexual development problems, comparing 30 children with problems and 30 children without problems, measuring their levels of anxiety, depression, and childhood memories. The results showed that children with problems had more anxiety and more depression, which are probably linked to variables related to family dynamics. The authors draw attention to the importance of creating an emotionally stable environment for children with developmental sexual problems to regulate emotional problems.

The following study (Zheng et al.) evaluated 1,142 patients with erectile dysfunction from a hospital in China, with the objective of determining the predictors of the patient's health. Erectile function, physical pain, and frequent and prolonged urination were the assessed determinants, and the authors confirmed a nomogram to predict the low and high risk of disease in patients with erectile dysfunction.

The seventh study (Cervilla and Sierra) compared the differences between men and women regarding masturbation parameters and their relationship with satisfaction with orgasm. The study demonstrated several differences between men and women, including men who masturbated earlier for the first time, masturbated more frequently, and expressed greater solitary sexual desire. Women, on the other hand, demonstrated greater intensity in the subjective experience of orgasm. However, for both men and women, the affective dimension proved to be decisive in the use of masturbation, highlighting its importance in sexual functioning, even in a relational context.

A systematic review and meta-analyses on the effectiveness of school-based child sexual abuse intervention among school

children in the new millennium era was the topic of the eighth contribution (Che Yusof et al.). In total, 29 studies assessing knowledge, skills, and attitudes were analyzed, and the authors concluded that programs that work on these domains are effective, which translates into improved wellbeing of children victims of sexual abuse.

Finally, the last study (Mourikis et al.) was also a systematic review of adult sexual wellbeing and behavior during the COVID-19 pandemic. A total of 31,911 participants were assessed for changes in sexual functioning attributable to the COVID-19 pandemic. Data analysis models demonstrated the negative impact of the pandemic on female sexual function but not on male subjects.

We believe that the contributions compiled in this Research Topic are important reinforcements for the advancement of scientific knowledge in the field of psychosexual health, with implications for clinical practice. On the one hand, psychosexual health is an integral part of psychological wellbeing, and on the other hand, it is necessary that all technicians and professionals working in this area understand the challenges and concerns and accept these contributions as a form of continuous improvement of their integrative practices, improving their effectiveness. In fact, many professionals will be able to benefit from this integrative vision as it will allow a paradigm shift, focusing on the multidisciplinary aspects of human sexuality.

Author contributions

The author confirms being the sole contributor of this work and has approved it for publication.

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Conflict of interest

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Markers of Prenatal Androgen Exposure Correlate With Online Sexual Compulsivity and Erectile Function in Young Men

OPEN ACCESS

Verena N. Buchholz^{1*†}, Christiane Mühle^{1†}, Cohort Study on Substance Use Risk Factors, Johannes Kornhuber^{1†} and Bernd Lenz^{1,2†}

Edited by:

Yasser Khazaal, University of Lausanne, Switzerland

Reviewed by:

Deena Marie Walker, Oregon Health and Science University, United States Louise Penzenstadler, Geneva University Hospitals (HUG), Switzerland

*Correspondence:

Verena N. Buchholz VerenaNadine.Buchholz@ uk-erlangen.de

†ORCID:

Verena N. Buchholz orcid.org/0000-0001-6607-8490 Christiane Mühle orcid.org/0000-0001-7517-9154 Johannes Kornhuber orcid.org/0000-0002-8096-3987 Bernd Lenz orcid.org/0000-0001-6086-0924

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Pornography addiction and sexual dysfunction are increasingly prevalent in young men. Previous studies suggest that prenatal androgen exposure plays a role in addiction and sexual functionality. Here, we tested whether lower second-to-fourth finger length ratio (2D:4D) and later age at spermarche, both putative indicators of higher androgen levels *in utero*, correlate with online sexual compulsivity (OSC scale of ISST), erectile function (IIEF-5), and ejaculatory control (PEPA) in 4,370 young men (age IQR: 25–26 years) of the Cohort Study on Substance Use Risk Factors. Statistical analyses revealed that lower 2D:4D correlated with higher scores on the OSC scale. Moreover, higher age at spermarche correlated with higher OSC scores and decreased erectile function. Interestingly, OSC severity, but not the frequency of pornography use, correlated negatively with erectile function and ejaculatory control. This is the first study to associate two independent proxies of prenatal testosterone level with OSC. These findings provide novel insight into intrauterine predisposition of sexual behavior and related sexual function in adulthood.

Keywords: prenatal androgen load, 2D:4D, digit ratio, spermarche, pornography addiction, premature ejaculation, erectile function, behavioral addiction

INTRODUCTION

Mannheim, Heidelberg University, Mannheim, Germany

A growing body of research supports that pornography addiction causes a great burden particularly to young males (1, 2). However, due to different conceptional categorizations and self-report bias, prevalence estimates are imprecise. Today, little is known about the biological mechanisms underlying pornography addiction.

Excessive pornography use is considered to promote sexual dysfunctions [for review, see (3)]. Erectile dysfunction affects primarily men above 40 years of age with previously reported prevalence rates of 1–10% in younger men and 50–100% in males older than 70 years (4). However, psychogenic erectile dysfunction in men under 40 years has risen sharply in the last decade up to rates as high as 14–28% in Europeans aged 18–40 years (5–7). The drastic worldwide increase of pornography use as sexual stimulation has been discussed to induce erectile dysfunction *via* alterations in the brain's motivational system (mesolimbic dopamine pathway) (3). Erections depend on dopaminergic neurons in the ventral tegmental area (VTA) and dopamine receptors in

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the nucleus accumbens (NAc) (3, 8, 9). This reward system is highly activated during pornography viewing with alterations in brain connectivity to the prefrontal cortex observed in subjects with pornography addiction compared with controls (10). Also, other addiction-related phenomena, like increased cue sensitivity, are observed in the brain responses of individuals addicted to pornography (11). Pornography has a high potential for addiction, considering its accessibility, affordability, and anonymity (2). Addiction to it can lead to a cascade of problems, ranging from erectile dysfunction to low sexual desire in partnered sex and relationship problems (3). Although clinical reports often suggest function improvement after abstinence from pornography, direct evidence of a causal effect is lacking (3), as is a scientific understanding of compulsive pornography use and its associated dysfunctions. For organic erectile dysfunction, in contrast, cardiovascular risk factors represent strong predictors (4).

Ejaculatory control also seems to be affected by excessive pornography consumption in hypersexual patients, resulting in reports of ejaculation difficulties in 33% of the patients (12). Premature ejaculation occurs frequently in adolescent males, especially during their first sexual encounters (13) and decreases over time as experience confers increased control. The criteria for premature ejaculatory control, according to the International Society of Sexual Medicine, are fulfilled by only 4–5% of the worldwide population. Furthermore, the perception of premature ejaculatory control is influenced by social conditioning through pornography consumption (14).

Males are more prone to pornography addiction than females (15). An Australian study found a self-reported prevalence rate of 4% in 9,963 men and only 1% in 10,131 women. This sexbased difference is also present in other non-substance-related and substance-related addictions, such as gambling (16), internet gaming (17, 18), and alcohol dependence (19). In general, sex differences originate from the sexual imbalance in X and Y chromosomes which determine gonadal development and later secretion of androgens and estrogens. During sensitive windows (e.g., prenatal, perinatal, and pubertal), these sex hormones lead to permanent organizational effects on brain and behavior which are discriminated from direct and reversible activational effects (20). Thus, studies have investigated the role of prenatal androgen exposure underlying addictive behavior. Indeed, initial associational evidence has suggested that video gaming addiction (21) and alcohol dependency are (22, 23) both related to prenatal androgen exposure. Together with genetic evidence linking sex hormone signaling to dependency (24-28), this suggests that androgen activity is involved in the pathology of addiction. Furthermore, a rodent study provides direct evidence that prenatal androgen receptor modulation affects alcohol consumption during adulthood (29). Human studies based on indirect markers of prenatal androgen exposure support its prenatal role in the development and maintenance of addictive behaviors during adulthood. Direct investigations of this issue in humans are hardly feasible due to ethical concerns and the long interval between the prenatal period and adulthood.

Research based on rodent experiments and human associational studies has identified markers of prenatal

androgen level, such as the second-to-fourth finger length ratio (2D:4D) [(30, 31); but see also: (32, 33)] and age at first ejaculation (spermarche) (34, 35). Human maternal plasma testosterone levels are negatively correlated with newborns' digit ratio in both sexes (36), and amniotic fluid testosterone levels are negatively associated with 2-year-olds' 2D:4D (37). A recent meta-analysis found lower 2D:4D (indicative of increased prenatal androgen exposure) in males with substancerelated and non-substance-related addictive behaviors (Hedge's g = -0.427) but not for females (Hedge's g = -0.260). This effect was stronger in the sub-analysis comparing dependent with non-dependent individuals (Hedge's g = -0.427) (38), which indicates that 2D:4D is more strongly related to addiction than to the frequency or amount of use. Moreover, lower 2D:4D associates with greater liver, muscle, and myelotoxic effects of alcohol and prospective hospital readmission in dependent patients (22). Alcohol-dependent males with lower 2D:4D are also more willing to purchase higher-priced alcoholic drinks (23). In parallel, alcohol-dependent patients (22) and individuals reporting binge drinking behavior (39) also report later age at spermarche. Experimental animal data show that prenatal androgen treatment increases pubertal onset age in male rats (35). Taken together, these data indicate that higher prenatal androgen exposure predisposes an individual to develop and maintain addictive disorders during adulthood. Interestingly, recent work suggests that stress, smoking, and alcohol use during pregnancy increases prenatal testosterone exposure, as indicated by lower 2D:4D in the human offspring (22, 40). Thus, maternal behavior might be an effective, novel target for addiction prevention among her offspring (41).

Alcohol use disorder and the problematic use of pornography overlap greatly in several aspects, which suggests common etiopathogenetic mechanisms (42). Sex-related rewards not only converge on the same neural pathway as drug rewards, but they also share the same molecular mediators and, most likely, the same neurons in the NAc, in contrast to other natural rewards like food (43). The incentive-salience model of addiction fits well with the dissociation observed in pornography addiction of increased craving ("wanting") and decreased pleasure from use ("liking") (44). Interestingly, especially the expectation to feel high following alcohol consumption correlates with lower 2D:4D (23). In addition to the molecular predispositions to addiction, pornography use might be more attractive for men with lower 2D:4D, as they have higher isolation intolerance (45), show more aggression or dominance behavior in some situations (46), and are more status-oriented (47). However, the role of intrauterine androgen level in online sexual compulsivity (OSC) and its related sexual dysfunctions have not yet been studied. Therefore, we tested our primary hypotheses that lower 2D:4D and later age at spermarche are related to OSC.

In addition to the reward system-related influences of prenatal androgen levels, prenatal androgen exposure shapes reproductive organs; i.e., lower 2D:4D (higher prenatal testosterone) correlates with greater penile length (48) and larger testes (49). Lower prenatal testosterone feminizes the reproductive organs (50, 51). Moreover, individuals with lifelong premature ejaculation have lower 2D:4D (52). Therefore, we also investigated whether 2D:4D

and age at spermarche are associated with erectile function and/or ejaculatory control.

METHODS

Demographic Data

The data analyzed here originated from the first to third survey waves of the longitudinal Cohort Study on Substance Use Risk Factors (C-SURF; www.c-surf.ch). From 2010 to 2012, 7,556 young males attending mandatory recruitment for the Swiss army provided written informed consent, of whom 5,987 men participated in Wave 1. In Wave 2, 5,036 males completed the questionnaire from 2012 to 2013, and Wave 3 spanned from 2016 to 2018 and included 5,160 males (see www.c-surf.ch). All analyzed data originated from Wave 3, except for the ejaculatory control and erectile function variables, which were assessed in Waves 1 and 2 only. We included young males who reported only being attracted to women, for several reasons: first, we wanted to maximize the homogeneity of our sample in terms of sexual behavior; second, one item was formulated specifically for vaginal penetration in the German version.

2D:4D

Similar to the methods described by (53) and (39), the participants were instructed to self-measure their 2D:4D (Questionnaire No. 3 ID: J18). They documented the lengths of the index and ring fingers in millimeters for their right and left hands separately. To eliminate inaccurate values, finger lengths below 10 mm and above 100 mm (53) and, subsequently, 2D:4D outside of the 2.5 and 97.5 percentiles (39, 54) were excluded, as previously described. We selected the mean of the right-hand and left-hand 2D:4D (Mean2D:4D) as the primary predictor and right-hand 2D:4D (R2D:4D), left-hand 2D:4D (L2D:4D), and the difference between R2D:4D and L2D:4D (2D:4Dr-l) as exploratory predictors.

Pubertal Onset Age

Self-reported pubertal onset age was controlled for time passed (years passed by since puberty) using partial correlation analysis, as recall biases are prevalent (55), i.e., the variance in the variable age at puberty onset that correlated with years since puberty (current age-puberty age) was removed. Furthermore, estimates below 9 were excluded, based on a previous report (56) and a previous analysis of 2D:4D and pubertal onset age (22).

OSC

The Internet Sex Screening Test (ISST; http://www.recoveryzone.com/tests/sex-addiction/ISST/index.php, developed by Delmonico, 1997) is a self-administered screening instrument that identifies clinically problematic sexual internet-based behavior. Factor analysis of the ISST data identified five factors: OSC, online sexual behavior-social, online sexual behavior-isolated, online sexual spending, and interest in online sexual behavior (57). The OSC subscale was included in the C-SURF questionnaire, consisting of six binary (yes/no) item. Subjects who did not visit a pornographic web site within the past 12 months (22.4%, n=1,064) were excluded from the analysis.

As clinically relevant cut-off scores do not yet exist and little research is available on the matter, we decided to use the sum score as a continuous variable in our analysis.

Pornography Consumption

Data from two items were available: one on the frequency of use (i.e., consumption days per month) and one on the duration of each use. In our cohort, the interquartile range (IQR) of consumption days was 3 to 15 days per month. Duration of the use: almost none, 1 to $<2\,\mathrm{h}, 2$ to $<3\,\mathrm{h}, 3$ to $<4\,\mathrm{h}, 4\,\mathrm{h},$ or more. We considered frequency to be more informative here, as the variability in consumption time was low, with 90% self-reporting $<1\,\mathrm{h}.$

Erectile Function

The International Index of Erectile Function (IIEF-5) Questionnaire consists of five items, scored using a five-point Likert scale. How do you rate your confidence that you could get and keep an erection? When you had erections with sexual stimulation, how often were your erections hard enough for penetration (entering of the penis into the vagina)? During sexual intercourse, how often were you able to maintain your erection after you had penetrated your partner? During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse? When you attempted sexual intercourse, how often was it satisfactory for you? The sum score was coded as a continuous variable for correlation analysis.

Ejaculatory Control

One item (five-point Likert scale) from the Premature Ejaculation Prevalence and Attitude (PEPA) survey was used (58): Within the last 6 months, how do you rate your control over ejaculation during partnered sex?

Ethical Approval

All subjects provided written informed consent prior to their inclusion in the original study. This study was approved by the Ethics Committee for Clinical Research of Lausanne University Medical School (Protocol No. 15/07).

Statistical Analyses

All data were analyzed using IBM SPSS Statistics version 24 for Windows (SPSS Inc., Chicago, IL, USA). When data points were missing, the study subject was excluded from the specific analysis (the number of individuals included in each analysis is reported as N). Descriptive statistics were expressed in frequencies, medians, and IQRs. We used the Wilcoxon signed-rank test to compare the dependent groups. Correlations were identified using Spearman's rank method, as the data were not normally distributed. p < 0.05 was considered to be statistically significant for two-sided tests. Semipartial correlations between residuals were performed to reveal the specific links connecting the variables. As described below, we also dissociated consumption-frequency-related effects from reported compulsivity by semipartial correlations as a *post-hoc* analysis.

TABLE 1 | Correlation between prenatal testosterone markers and OSC.

		osc	OSC (controlled)
Mean2D:4D	Coefficient	-0.042	-0.044
	р	0.015	0.011
	N	3276	3273
Pubertal onset age	Coefficient	-0.010	0.048
	p	0.556	0.004
	Ν	3682	3678
		$\begin{array}{ccc} & \rho & \\ N & \\ \text{Pubertal onset age} & \text{Coefficient} \\ & \rho & \end{array}$	Mean2D:4D Coefficient p -0.042 p 0.015 m 0.015 m 0.015 m 0.015 m 0.010 m 0.010 m 0.010 m 0.0556 m

2D:4D, second-to-fourth-finger length ratio; Mean2D:4D, mean of right-hand and left-hand 2D:4D; OSC, online sexual compulsivity; OSC (controlled), variance that correlated with consumption removed; p < 0.05 in bold print.

RESULTS

Cohort Demographics

After the step-wise exclusion of subjects who failed to meet the quality criteria of 2D:4D (n = 518) and/or pubertal onset age (N = 94) and who were not exclusively attracted to women (N = 534), the total cohort was characterized as follows: age 25 years (IQR 25-26, N = 4,370); body mass index 23.6 kg/m^2 (IQR 21.9-25.5, N = 4,362); 79.8% gainfully employed (N = 4,369); education: 3.0% secondary education, 1.2% basic vocational education, 34.9% secondary vocational/technical education, 4.4% community college, 11.1% vocational high school, 11.3% high school, 23.2% bachelor degree (university), 5.9% masters degree (university), 4.7% other (N = 4,358); marital status: 82.9% single, 5.3% married, 0.1% divorced, 11.5% not married, separated, or divorced but living together with a partner (e.g., in a registered partnership), 0.2% married but separated, 0.0% widowed (N = 4,363); 37.5% were still living with their parent(s). In the last 12 months, 59.9% had one sexual partner, 5.9% had none, 34.2% had two or more. Mean2D:4D was 0.981 (IQR 0.955-1.000, N = 4,177), R2D:4D 0.986 (IQR 0.951-1.000,N = 4,269), L2D:4D 0.986 (IQR 0.951–1.000 N = 4,278), 2D:4Dr-10.000 (IQR - 0.013 - 0.012, N = 4,177).

Of the pornography-consuming subjects, 41% gave at least one positive response to the OSC questions; 18.4% reported at least two problematic behaviors from the OSC. In our cohort, 41.3% reported at least mild erection problems, and 5% reported poor control over ejaculation during intercourse.

Prenatal Testosterone Markers and OSC

First, we tested our main hypothesis, stating that increased prenatal testosterone, as indicated by a lower Mean2D:4D and/or higher pubertal onset age, is associated with a higher OSC score in our cohort. While Mean2D:4D correlated significantly in the expected direction, the self-reported pubertal onset age did not (Table 1).

Next, we controlled for the actual consumption frequency in our dependent variable OSC, as more severe compulsivity was associated with increased use (Rho = 0.184, p < 0.001, N = 3,678), pubertal onset age was negatively correlated with consumption frequency (Rho = -0.124, p < 0.001, N = 3,680), but Mean2D:4D was not (Rho = 0.008, p = 0.647, N = 3,274) and we were specifically interested in the compulsivity aspect, given

TABLE 2 | Post hoc analysis of 2D:4D markers.

			osc	OSC (controlled)
Spearman-Rho	L2D:4D	Coefficient	-0.037	-0.037
		p	0.033	0.031
		N	3348	3345
	R2D:4D	Coefficient	-0032	-0.032
		p	0.064	0.066
		N	3348	3345
	2D:4Dr-I	Coefficient	0.019	0.014
		p	0.285	0.415
		N	3276	3273

2D:4D, second-to-fourth-finger length ratio; exploratory predictors: L2D:4D, left-hand 2D:4D; R2D:4D, right-hand 2D:4D; 2D:4Dr-l, difference between R2D:4D and L2D:4D; OSC, online sexual compulsivity; OSC (controlled), variance that correlated with consumption removed; p < 0.05 in bold print.

a certain consumption level. After correcting for the frequency of use, the OSC score correlated negatively with Mean2D:4D and positively with pubertal onset age (both indicative of higher prenatal testosterone level), thus supporting our primary hypothesis (**Table 1**).

In a *post-hoc* analysis, we explored relationships of OSC scores with R2D:4D, L2D:4D, and 2D:4Dr-l (**Table 2**). L2D:4D correlated significantly with OSC, while only a trend was observed for R2D:4D.

As vulnerability for mood disorders and traits like sensation seeking might be influenced by prenatal as well as pubertal androgen exposure which could mediate some of the observed effects, we performed an exploratory analysis on the available scores for major depression, MDI (59), bipolar disorder, MDQ (60), and sensation seeking, BSSS (61). Whereas Mean2D:4D did not significantly correlate with these measures respectively (Rho = -0.002, p = 0.922, N = 4,155; Rho = -0.015, p = 0.335, N = 4,161; Rho = 0.006, p = 0.698, N = 4,170), higher puberty onset age was associated with a lower number of symptoms respectively (Rho = -0.032, p = 0.029, N = 4,717; Rho = -0.050, p = 0.001, N = 4,720) and less sensation seeking (Rho = -0.118, p < 0.001, N = 4,736).

Prenatal Testosterone Markers and Sexual Dysfunction

To investigate the influence of prenatal testosterone on sexual dysfunction and test our secondary hypotheses, we first explored the development of ejaculatory control and erectile function over time (i.e., from Wave 1 to Wave 2, since sexual dysfunction was not assessed in Wave 3). There was a significant increase in erectile function over time but no change in ejaculatory control $(Z=-5.76,\ p<0.001;\ Z=-2.15,\ p=0.830)$. Therefore, we controlled our dependent variable erectile function (from Wave 2) for age. Pubertal onset age correlated negatively with erectile function (controlled) but not with ejaculatory control; Mean2D:4D did not correlate significantly with either; see **Table 3**.

TABLE 3 | Prenatal testosterone markers and sexual functions.

			Erectile function (controlled)	Ejaculatory control
Spearman-Rho	Mean2D:4D	Coefficient	-0.012	0.002
		p	0.501	0.904
		N	3321	3325
	Pubertal onset age	Coefficient	-0.143	-0.005
		p	<0.001	0.782
		N	3771	3781

2D:4D, second-to-fourth-finger length ratio; Mean2D:4D; controlled, variance that correlated with age removed; p < 0.05 in bold print.

TABLE 4 | Pornography use and sexual functions.

			Erectile function (controlled)	Ejaculatory control
Spearman-Rho	OSC	Coefficient	-0.128	-0.062
		р	<0.001	0.002
		N	2949	2599
	OSC (controlled)	Coefficient	-0.129	-0.062
		p	<0.001	0.002
		N	2945	2596
	Frequency of use	Coefficient	0.011	-0.004
	(days/month)	р	0.540	0.829
		N	2946	2596
	Hours of use	Coefficient	-0.014	-0.016
	(on days of use)	р	0.444	0.414
		N	2949	2598

Erectile function (controlled), variance that correlated with age removed; OSC, online sexual compulsivity; OSC (controlled), variance that correlated with consumption removed; p < 0.05 in bold print.

Given suggestions in the literature that pornography consumption influences sexual dysfunction, we explored the relationships between pornography use, OSC, and sexual functions. Interestingly, pornography use frequency did not significantly correlate with erectile function, whereas OSC did, with more compulsive symptoms related to less ejaculatory control and less erectile function (**Table 4**); moreover, the hours spent on pornography in each occasion did not correlate significantly with either.

DISCUSSION

Here we describe the first evidence of the influence of prenatal androgen exposure on OSC behavior in males during young adulthood. Our data confirmed our primary hypotheses that lower 2D:4D and later age at spermarche—both independently indicative of higher prenatal testosterone levels—were significantly (although with small effect size) associated with stronger OSC, despite reliable measurements of finger length from multiple expert raters and clinical data on time of puberty onset being unavailable.

These findings align well with the existing knowledge. The male sexual response and associated natural reward are mediated via mesolimbic dopamine signaling in the VTA and the NAc (8). This circuit forms the core of the reward system and, as such, it does not only mediate sexual reward (62) but also underlies substance addictions, such as alcoholism (63). Prenatal testosterone is suggested to affect the onset and course of alcohol dependence (22), and a study in mice found that prenatal modulation of androgen receptors affects cerebral dopamine, serotonin, and noradrenaline neurotransmitter levels in adulthood (29). In female sheep, prenatal testosterone positively correlates with the number of tyrosine hydroxylase-immunoreactive cells in the VTA (64). Furthermore, methamphetamine addiction is also mediated by the same neural substrates as sexual stimulation (65). Repeated sexual behaviors and repeated psychostimulant administration both induce the up-regulation of DeltaFosB, thereby sensitizing the mesolimbic pathway (43). Gene expression of the mu-opioid receptor, a key player in addiction pathology, appears to be sex-specifically altered by prenatal testosterone intervention (29). Moreover, the A118G variant of the mu-opioid receptor gene interacts with 2D:4D to predict alcohol dependence (66).

Whereas, OSC was associated with higher prenatal testosterone levels indicated by both markers, use frequency showed the opposite relationship with pubertal onset age, which might be a social peer group effect. A recent meta-analysis also concluded that 2D:4D relates more to addiction phenotypes than the frequency or amount of use (38). In summary, our findings both reinforce and further our understanding of drug addiction and addiction to sexual reward, namely, that they may share the same neural circuits that are vulnerable to prenatal androgen levels.

Our secondary hypothesis, that increased prenatal testosterone may also affect sexual functions, was only partially supported by the data. We found a significant correlation between erectile function and time of puberty, with later onset being associated with less function; however, we did not find a link to Mean2D:4D. This inconsistency may be due to the different prenatal windows during which 2D:4D and pubertal timing are determined. Two independent studies have provided evidence of 2D:4D development occurring during early pregnancy (67, 68). In contrast, when pubertal timing is exactly determined remains unclear, and it can be assumed that pubertal timing is not only a marker for prenatal androgen exposure but also influences brain organization during adolescence.

Additional research is needed to clarify whether the organizational influence of prenatal androgen on the reward system mediates this link, whether increased peripheral androgen receptors, which are involved in erectile function (69) play a role, or whether erectile dysfunction is a secondary effect of OSC and, therefore, arises from increased consumption of pornographic content and impacts sexual arousal during partnered sex *via* associated motivational aspects.

In the future, validated screening tools are required to disentangle the origins of sexual dysfunction related to

pornography addiction by accurately assessing the context of sexual difficulties, progression of OSC, and pornography consumption over time. Also, developmental factors should be considered, as the reward circuit and its prefrontal control are highly vulnerable during adolescence (70). Additionally, experimental manipulation of consumption frequency, clinical interventions based on pornography abstinence, and investigation of pharmacological effects on dysfunction should be carefully investigated in the future, to further the understanding of the underlying etiology.

Ejaculatory control did not correlate with either prenatal testosterone marker. Given a previous study reporting a link between prenatal testosterone and premature ejaculation (52), this finding was initially unexpected. However, the cohort involved in that study differed from ours in several ways. First, the Bolat et al. (52) study only included patients with a lifelong history of premature ejaculation issues. Second, their cohort was older (mean age 40 years). Third, we do not know how experienced the subjects of our study were in controlling ejaculation during intercourse, as 82% are single, which limits experiential learning with a confidant. Fourth, pornography-related behavior was not assessed in our study.

Pornography-related sexual dysfunctions are not yet well-understood. A recent review describes pornography, its availability, and many different forms as a supernatural stimulus, which, in the long-term, leads to problems achieving sufficient stimulation in natural (partnered) settings. This, in turn, can cause several issues, from erectile dysfunction during partnered intercourse and delayed ejaculation, to being unable to ejaculate entirely during partnered sex (3). We did not have sufficient data in the present study to distinguish between premature and delayed ejaculation, as both are covered by the item about ejaculatory control, which was negatively associated with OSC. A recently published model describing users' need for more extreme material over time to be able to ejaculate has not yet been verified (71), and increased tolerance is currently not yet well-defined for pornography addiction. However, pornography consumption influences subjective and self-reported estimates of typical latency times.

We find it very interesting that OSC, not pornography use itself, was associated with less ejaculatory control and less erectile function; this suggests a tight link between OSC and sexual dysfunction *via* alterations to the reward system as opposed to social associative mechanisms. Also here, more research is needed to disentangle cause and effect.

The present study is subject to several limitations. 2D:4D was self-quantified, and frequencies of pornography use, erectile function, and ejaculatory control were self-reported. Pornography addiction is not yet formally recognized as a behavioral addiction, and, therefore, its definition varies (72). Here, we focused on the OSC subscale of the ISST, representing the compulsivity aspect of this behavioral addiction. Moreover, we investigated a homogeneous cohort of young, heterosexual males, most of whom were Caucasian and single; therefore,

our findings cannot be generalized to other age groups, sexual orientations, ethnicities, or females. Finally, 2D:4D and puberty onset have limited validity as markers for prenatal androgen exposure (33, 38, 73), and it is likely that pubertal timing also directly affects brain organization, as puberty is also a sensitive time window (74). Therefore, our finding of an association between pubertal timing and OSC may not only be a result of prenatal but also pubertal androgen exposure associated vulnerabilities.

In conclusion, higher prenatal androgen levels (indicated by two independent markers) are associated with more compulsive pornography use. A more compulsive use in turn is associated with less erectile function and low ejaculatory control in young men. In addition, less erectile function was associated with a higher pubertal onset age, which may indicate higher prenatal androgen levels. Thus, the etiology of erectile dysfunction and its sharp rise in prevalence within the last decade might involve an interaction of a prenatal predisposition to develop sexual online compulsivity and/or erectile dysfunction and increased availability of pornographic content. Future studies are encouraged to disentangle the relative contribution of these factors and further the understanding of this behavioral addiction and related sexual problems. These insights could help to develop prevention programs, targeting either subjects at risk to develop this addiction or mothers whose prenatal testosterone levels are high.

DATA AVAILABILITY STATEMENT

The datasets generated for this study are available on request to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee for Clinical Research of Lausanne University Medical School (Protocol No. 15/07). The patients/participants provided their written informed consent to participate in this study.

Members of the Cohort Study on Substance Use Risk Factors

Gerhard Gmel: Addiction Medicine, Lausanne University Hospital CHUV, University of Lausanne, Lausanne, Switzerland; Addiction Switzerland, Lausanne, Switzerland; Centre for Addiction and Mental Health, Toronto, ON, Canada; University of the West of England, Frenchay Campus, Bristol, United Kingdom (Gerhard.Gmel@chuv.ch). Meichun Mohler-Kuo: La Source, School of Nursing Sciences, HES-SO University of Applied Sciences and Arts of Western Switzerland, Lausanne, Switzerland (m.mohler-kuo@ecolelasource.ch). Simon Foster: Institut für Epidemiologie, Biostatistik Hirschengraben, Prävention, Zürich, Switzerland (simon.foster@kjpd.uzh.ch). Simon Marmet: Addiction Medicine, Lausanne University Hospital CHUV, University of Lausanne, Lausanne, Switzerland (simon.marmet@chuv.ch). Joseph Studer: Addiction Medicine, Lausanne University Hospital CHUV, University of Lausanne, Lausanne, Switzerland (Joseph.Studer@chuv.ch).

AUTHOR CONTRIBUTIONS

VB and BL conceived and designed the research, analyzed the data, and wrote the manuscript. GG, MM, SM, SF, and JS performed the experiments. CM and JK commented on the manuscript and provided the intellectual input. All authors contributed to the article and approved the submitted version.

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Psychosocial Determinants of Marital Satisfaction Among Gynecologic Cancer Survivors in Malaysia

Sidi Hatta¹, Luke Sy-Cherng Woon^{1*}, Nik Mohd Nor Nik Sumayyah² and Shafiee Mohamad Nasir²

¹ Department of Psychiatry, Faculty of Medicine, National University of Malaysia, Kuala Lumpur, Malaysia, ² Department of Obstetrics and Gynecology, Faculty of Medicine, National University of Malaysia, Kuala Lumpur, Malaysia

Introduction: Marital issues among gynecologic cancer survivors are common but complex. This study aimed to investigate the relationship between sociodemographic and clinical factors, including sexual dysfunction and marital satisfaction among Malaysian gynecologic cancer survivors.

Methods: A cross-sectional survey of married women with gynecologic cancers was conducted at a Malaysian university hospital. Sociodemographic and clinical data were gathered. Sexual dysfunction was measured using the Malay Version Female Sexual Function Index (MVFSFI), while marital satisfaction was evaluated with the Malay Version Golombok Rust Inventory for Marital Satisfaction (MVGRIMS).

Results: A total of 116 patients participated in this study. The median age was 59.0 years (Interquartile range, IQR: 49.0–67.0 years); the median duration of marriage was 32 years (IQR: 20.0–40.8 years). 80.2% had a secondary and lower level of education. 37.9% of study subjects (n=44) reported poor-and below-levels of marital satisfaction, which was equivalent to MVGRIMS transformed scores of >5. The median FSFI total score was 49.9 (IQR: 2.0–63.0). MVGRIMS transformed score correlated significantly with all MVFSFI sub-scores. In logistic regression, lower educational levels were associated with poor marital satisfaction [primary, (adjusted Odds Ratio) aOR = 12.67, 95% CI: 1.40–114.87; secondary: aOR = 11.52, 95% CI: 1.39–95.72], while higher MVFSFI total score reduced the likelihood of poor marital satisfaction (aOR = 0.979, 95% CI: 0.964–0.994).

Conclusion: Both sexual dysfunction and low education level may affect marital satisfaction among gynecologic cancer survivors. Targeted efforts focusing on sex education for patients may help to improve marital satisfaction.

Keywords: cancer survivors, educational achievement, gynecologic neoplasms, marital relationship, sexual dysfunctions

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*Correspondence:

Luke Sy-Cherng Woon lukewoon@ukm.edu.my

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INTRODUCTION

The diagnosis of gynecologic cancer and implications from the ensuing therapy profoundly alter the lives of women with cancers. Survivors of gynecologic cancers often encounter psychosocial issues, as manifested in the areas of group functioning, and role-taking, relationship with family, and marital relationship (1).

Marital issues among gynecologic cancer survivors are common. In a study, among women with gynecologic cancer who were in relationships, 27% encountered marital dysfunction (2). Such marital problems are often complex, involving various factors. For many survivors, sexual dysfunction issues seem to be the most distressing, as impaired sexual performance is perceived as jeopardizing their relationship with their partners (3). Many gynecologic cancer patients consciously keep their physical and emotional distance from their spouses to pre-empt possible rejection (4).

A recent study focusing on the relationship between sexual dysfunction and the quality of marital relationships in breast and genital cancer women found that recent sexual dysfunction had significantly poorer relationships with their spouses (5). Conversely, women who had a more intimate relationship with their partners experienced better sex life (6).

Sociodemographic factors are important contributing factors to the occurrence of gynecologic cancers. For instance, low education level, low-income level, and low occupation level (i.e., manual/unskilled labor) are risk factors of cervical cancer (7, 8). Moreover, sociodemographic factors also contribute to poor quality of life and psychosocial adjustment in gynecologic cancer survivors. Such factors include lower education, poor social support, and lower levels of religious belief (9). There is also evidence to suggest clinical factors such as treatment modalities may affect psychosocial adjustment in patients (10, 11).

Not many studies have been conducted in the Malaysian context to address issues related to marital satisfaction in a conservative Malaysian community (12). Indeed, to the best of our knowledge, no study was conducted on marital satisfaction among gynecological cancer survivors. Mustafa et al. outlined issues on the conventional values about relationships, emphasizing the stability of the relationship and belief in traditional gender role expectations in Malaysian middle-aged women. In their study, couples tend to spend their time together and avoid arguments and conflicts in their daily life (12). Sidi et al. found that discussing sex openly may be taboo but emphasized the importance of researching in this field of specialty to improve the betterment and quality of life among Malaysian women (13, 14). Sidi et al. reported that sexual topic is well-received in the suburban Malaysian society during their study on the validation of the Female Sexual Functioning Index (FSFI), especially at the face and content validity of the questionnaire (15).

The main objective of this study was to investigate the level of marital satisfaction among a group of gynecologic cancer survivors in Malaysia. The secondary objective was to explore the relationship between psychosocial and clinical factors, including sexual dysfunction, with marital satisfaction among gynecologic cancer survivors. We hypothesized that

marital dissatisfaction was prevalent among gynecologic cancer survivors, and that it was associated with sexual dysfunction and other psychosocial determinants.

MATERIALS AND METHODS

This was a cross-sectional study. The study population was patients with gynecologic cancer who received treatment at the National University of Malaysia Medical Centre located at Bandar Tun Razak, Cheras in metropolitan Kuala Lumpur, Malaysia. The study subjects were recruited via convenience sampling from June 2017 to March 2020. The inclusion criteria were: (1) Malaysian citizens; (2) age of at least 18 years old; (3) married; (4) diagnosed of gynecologic cancer; and (5) had completed treatment for a minimum of 3 months. Disease progression on treatment and significant amnesia were the exclusion criteria. Sample size calculation was based on the estimated prevalence of marital dissatisfaction of 40% (16) and the study population of 160 (based on clinic records). Using the formula for sample size calculation for prevalence studies with finite population correction (precision = 0.05), the sample size required was 112.

Informed consent was obtained from all eligible participants before their participation. They were asked to fill up a self-administered questionnaire on sociodemographic data, including age, ethnicity, marital status, number of children, level of education, and employment status. Existing medical records were accessed to trace clinical data on the type and stage of cancer, duration of disease, type of treatment received, and duration of treatment completion. In addition, two validated instruments were employed to evaluate sexual dysfunction and marital satisfaction, respectively. Sexual dysfunction was measured using the Malay Version Female Sexual Function Index (MVFSFI), while marital satisfaction was evaluated with the Malay Version Golombok Rust Inventory for Marital Satisfaction (MVGRIMS).

The FSFI is a brief and reliable self-report measure of female sexual function developed by Rosen et al. (17). This questionnaire contains 19 items covering six domains of female sexual dysfunction, i.e., desire, subjective arousal, lubrication, orgasm, satisfaction, and pain. The lower the scores, the higher likelihood the women would suffer from sexual dysfunction. The Malay version of FSFI (MVFSFI) used in this study has been validated in the Malaysian population (15). The instrument demonstrated good face, content, and criterion validity. It also showed a high level of test-retest reliability. Regarding the reliability, the strongest correlation (0.973) was demonstrated for the domain of satisfaction in MVFSI and the weakest correlation for the domain of arousal (0.767). Total score \leq 55 and above was found to be the suitable cut-off point to distinguish between women with sexual dysfunction and those without, with a sensitivity of 99% and a specificity of 97%.

The Golombok-Rust Inventory of Marital State (GRIMS) by Rust et al. is among the most used instruments in research to assess marital satisfaction (18). It is a 28-item structured questionnaire covering the degree of dependence and independence, warmth, love and hostility, trust and respect,

TABLE 1 | Characteristics of the study subjects (N = 116).

Variable	n	Percentage
Age (years)	59.0 ^a	49.0-67.0 ^b
Years of marriage	32.0 ^a	20.0-40.8 ^b
Employment		
Employed	29	25.0
Unemployed	27	23.3
Retired	21	18.1
Homemaker	39	33.6
Education level		
Primary	32	27.6
Secondary	61	52.6
Tertiary	23	19.8
Ethnicity		
Malay	79	68.1
Chinese	33	28.4
Indian	4	3.4
Number of children	3.0 ^a	1.0-4.0 ^b
Cancer type		
Endometrial	48	41.4
Cervical	37	31.9
Ovarian	31	26.7
FIGO staging		
Stage 1	58	50.0
Stage 2	21	18.1
Stage 3	30	25.9
Stage 4	7	6.0
Treatment		
Surgery only	36	31.1
Surgery and chemotherapy	35	30.2
Surgery and radiotherapy	19	16.4
Surgery and chemoradiotherapy	19	16.4
Chemotherapy and radiotherapy	5	4.3
Radiotherapy only	2	1.7
Years of diagnosis	3.5ª	2.0-7.8 ^b
Years of last treatment ($n = 115$)	2.0 ^a	0.5-6.0 ^b

^aMedian; ^binterquartile range.

coping with problems, and crisis. Each item has a four-point Likert scale, from score 0 for 'Strongly disagree' to score 3 for 'Strongly agree'. A total score is then computed (range: 0–84), with a high score indicating a likelihood of marital dissatisfaction. The raw GRIMS score is transformed into a standardized GRIMS score ranging from 1 to 9, with a cutoff point of 5. A total transformed score from 6 to 9 represents marital dissatisfaction ranging from poor to very severe (19). The Malay version of GRIMS (MVGRIMS) was used in the present study with the permission of the original author. Validation of this instrument has been done in Malaysia. The reliability of the GRIMS is 0.91 for men and 0.87 for women, with good validity under various situations (16, 20).

Statistical analysis was conducted using the Statistical Package for Social Science version 26.0 (IBM Corp., Armonk, NY,

USA). Descriptive statistics of the study subjects were generated. The normality test showed that the continuous data were not normally distributed (Kolmogorov-Smirnov test, p < 0.05). Categorical variables were reported in frequency and percentage, while continuous variables were in median and interquartile range (IQR). Correlations between MVGRIMS score and MVFSFI total and sub-scores were measured using Spearman's correlation coefficient. MVGRIMS scores were divided into two categories. A score of <5 represented "average and above" marital satisfaction, and a score of >5 represented "poor and below" marital satisfaction. Bivariate analysis was run to examine the differences between the "average and above" group and the "poor and below" group with regards to demographic, social, and clinical characteristics, using the chi-square test or Fisher's exact test for categorical variables and Mann-Whitney U-test for continuous variables. Significant variables were then included in a stepwise multiple logistic regression model as independent variables to look for factors that were significantly associated with marital dissatisfaction. The logistic regression model displayed a good fit with a non-significant Hosmer-Lemeshow goodness-offit test (p = 0.730). The significance level (alpha) for all statistical tests was set at p < 0.05.

Ethics approval (Code: FF-2018-203) was granted by the Research Ethics Committee of the National University of Malaysia for this study before its commencement. The respondents were given options to seek professional help if they are having marital dissatisfaction and sexual dysfunction.

RESULTS

The sociodemographic and clinical characteristics of the study subjects are shown in **Table 1**. A total of 116 patients participated in this study. The median age was 59.0 years (IQR: 49.0–67.0 years); the median duration of marriage was 32 years (IQR: 20.0–40.8 years). 80.2% had a secondary and lower level of education. About two-thirds were of Malay ethnicity. The most common type of gynecologic cancer was endometrial cancer at 41.4%. Most were at the early stages of cancer according to the International Federation of Gynecology and Obstetrics (FIGO) staging system, with 50% at FIGO stage 1. The majority received either surgery alone (31.1%) or a combination of surgery and chemotherapy (30.2%) as their treatment.

The levels of marital satisfaction among the subjects according to the MVGRIMS transformed scores are displayed in **Table 2**, showing a wide range of marital satisfaction. When divided into two categories, 62.1% (n=72) of study subjects had average and above levels of marital satisfaction, with the remaining (37.9%, n=44) reporting poor and below levels of marital satisfaction, equivalent to MVGRIMS transformed scores of >5. The transformed GRIMS scores of 1 should be treated cautiously according to the instrument's authors (16). Nonetheless, there was only one such score in the study sample. The median FSFI total score was FSFI 49.9 (IQR: 2.0-63.0). When the correlations between MVGRIMS score and MVFSFI scores were examined, the MVGRIMS score was inversely correlated with all MVFSFI sub-scores and total scores. The correlation

TABLE 2 | Levels of marital satisfaction among the subjects.

Variable	n	Percentage
Very good	19	16.4
Good	22	19.0
Above average	15	12.9
Average	15	12.9
Poor	20	17.2
Bad	14	12.1
Severe problems	4	3.4
Very severe problems	6	5.2
Score of "1"	1	0.9

TABLE 3 | Correlations between MVGRIMS transformed score and MVFSFI scores.

Variable	Spearman's rho	p-value
MVFSFI Desire	-0.390	<0.001*
2. MVFSFI Arousal	-0.387	<0.001*
3. MVFSFI Lubrication	-0.286	0.002*
4. MVFSFI Orgasm	-0.342	<0.001*
5. MVFSFI Satisfaction	-0.367	<0.001*
6. MVFSFI Pain	-0.315	0.001*
7. MVFSFI Total Score	-0.380	<0.001*

^{*}Statistically significant.

coefficients were statistically significant, ranging from -0.286 to -0.390, indicating a moderate negative relationship between the severity of sexual dysfunction and the level of marital satisfaction (**Table 3**).

The subsequent bivariate analysis compared study subjects with better (average and above) and those with worse (poor and below) levels of marital satisfaction (Table 4). Older age, longer duration of the marriage, and lower MVFSFI scores were associated with worse levels of marital satisfaction. Additionally, employment status, education level, ethnicity, and cancer type were also significant. Therefore, age, duration of the marriage, MVFSFI score, employment status, education level, ethnicity, and cancer type (endometrial, cervical, or ovarian) were included in the stepwise multiple logistic regression analysis. For MVFSFI scores, only the total score was included as the sub-scores were highly correlated with each other and the total score. In the final logistic regression analysis, after controlling for confounders, lower educational levels were found to be significantly associated with poor marital satisfaction (Primary education, aOR = 12.67, 95% CI: 1.40-114.87; secondary education: aOR = 11.52, 95% CI: 1.39-95.72), while higher MVFSFI total score significantly reduced the likelihood of poor marital satisfaction (aOR = 0.979, 95% CI: 0.964-0.994) (Table 5).

Post-hoc analyses were conducted to test whether the inverse association between sexual dysfunction and marital satisfaction only occurred among study subjects with lower educational levels (secondary and below) and not those with tertiary education. A

statistically significant correlation was found between MVFSFI total score and MVGRIMS score among participants with primary and secondary education, Spearman's rho = -0.350(p = 0.001). Nonetheless, the Spearman's correlation coefficient between FSFI total score and GRIMS score among participants with tertiary education was not significant (Spearman's rho = -0.166, p = 0.450). To further investigate the possibility of education level moderating the relationship between sexual dysfunction and marital dissatisfaction, a moderated regression analysis was performed using PROCESS version 3.5. The outcome variable for analysis was MVGRIMS transformed score. The predictor variable was FSFI total score. The moderator variable was education level. The interaction between FSFI total score and education level was statistically insignificant (B = 0.0088, 95% CI: -0.0075 to 0.0252, p = 0.2856). Hence, education level did not moderate the relationship between sexual dysfunction and marital dissatisfaction. Education level and sexual dysfunction were independently associated with marital dissatisfaction.

DISCUSSION

In this study, we found that lower levels of education and lower MVFSFI scores (indicating greater degrees of sexual dysfunction) were significant factors associated with poor marital satisfaction, as defined by an MVGRIMS transformed score of >5. Furthermore, additional analyses confirmed that education level and sexual dysfunction had distinct associations with marital dissatisfaction.

Our finding that sexual dysfunction was associated significantly with martial dissatisfaction agrees with the previous study by (5) among breast and genital cancer patients. They found that patients who fulfilled the criteria of sexual dysfunction had significantly lower mean scores for quality of relationship with spouse compared with those without sexual dysfunction. It is speculated that the relationship between sexual function and marital satisfaction among cancer patients can be two-way. Women with a closer relationship with their spouses may have a better sex life with their husbands, thereby reporting less sexual dysfunction (6). Conversely, due to the impact of the illness and the consequences of treatment, patients may experience emotional and physical symptoms that interfere with their sexual desire and sexual function, resulting in reduced sexual intercourse with their husbands. These symptoms may consequently contribute to relationship problems and marital dissatisfaction (21). A study by Fahami et al. (5) found that the quality of a marital relationship is one of the crucial factors predicting sexual functioning, which varies among different types of cancers. A correlational study among more than 100 patients with breast and gynecological cancers concluded that there was a significant correlation between sexual functioning and quality of marital relationship. For couples who are longer in a relationship, as seen in the long median duration of marriage of 32 years in our study, addressing both issues on marital and sexual relationship is important for a better quality of life and health care.

TABLE 4 | Comparisons between study subjects with better and with worse marital satisfaction.

Variable		Marital sa	atisfaction		<i>p</i> -value
		Better		Worse	
	N	Percentage	n	Percentage	
Age (years) ^a	56.5 ^d	46.0-64.0 ^e	63.0 ^d	57.0-69.0 ^e	0.001*
Years of marriage ^a	28.5 ^d	18.0-37.0 ^e	40.0 ^d	28.5-44.0 ^e	0.001*
Employment ^b					
Employed	25	34.7	4	9.1	0.004*
Unemployed	13	18.1	14	31.8	
Retired	15	20.8	6	13.6	
Homemaker	19	26.4	20	45.5	
Education level ^b					
Primary	14	19.4	18	40.9	<0.001*
Secondary	36	50.0	25	56.8	
Tertiary	22	30.6	1	2.3	
Ethnicity ^c					
Malay	56	77.8	23	52.3	0.017*
Chinese	14	19.4	19	43.2	0.01.
Indian	2	2.8	2	4.5	
Number of childrena	2.5 ^d	1.0–4.0e	3.0 ^d	1.3–4.0e	0.249
Cancer type ^b	2.0	1.0 1.0	0.0	1.0 1.0	0.210
Endometrial	28	38.9	20	45.5	0.036*
Cervical	19	26.4	18	40.9	0.000
Ovarian	25	34.7	6	13.6	
FIGO staging ^c	25	54.7	0	10.0	
	35	48.6	23	52.3	0.757
Stage 1 Stage 2	12	16.7	9	20.5	0.757
-					
Stage 3	21	29.2	9	20.5	
Stage 4	4	5.6	3	6.8	
Treatment	00	00.0		04.0	0.110
Surgery only	22	30.6	14	31.8	0.112
Surgery and chemotherapy	27	37.5	8	18.2	
Surgery and radiotherapy	10	13.9	9	20.5	
Surgery and chemoradiotherapy	10	13.9	9	20.5	
Chemotherapy and radiotherapy	3	4.2	2	4.5	
Radiotherapy only	0	0.0	2	4.5	
Years of diagnosisa	4.0 ^d	2.0-7.0 ^e	2.5 ^d	2.0-8.0 ^e	0.62
Years of last treatmenta	2.0 ^d	0.4-6.0 ^e	2.0 ^d	0.6–5.8 ^e	0.947
MVFSFI scores					
Desire	5.0 ^d	3.0-6.0 ^e	2.0 ^d	2.0-4.0 ^e	<0.001*
Arousal	12.0 ^d	1.0-14.0 ^e	0.0 ^d	0.0-7.8 ^e	<0.001*
Lubrication	11.0 ^d	0.0-15.0 ^e	0.0 ^d	0.0-10.0 ^e	<0.001*
Orgasm	9.0 ^d	0.0-11.0 ^e	0.0 ^d	0.0-7.0 ^e	<0.001*
Satisfaction	10.0 ^d	0.0-12.8 ^e	0.0 ^d	0.0-7.8 ^e	<0.001*
Pain	9.0 ^d	0.0-12.0 ^e	0.0 ^d	0.0-9.0 ^e	0.001*
Total	57.5 ^d	5.3-68.3 ^e	2.0 ^d	2.0-50.5 ^e	< 0.001*

^aMann-Whitney U test; ^bChi-squared test; ^cFisher's exact test; ^dmedian; ^einterquartile range.

The prevalence of female sexual dysfunction among patients with a gynecologic cancer was as high as 78.44% (95 % CI 68.36-88.52%) as measured using the FSFI in a meta-analysis

(22). Treatments of gynecologic cancers are prone to cause sexual dysfunction (23). Surgical procedures for gynecologic cancers may result in body image changes, pain, and problem in attaining

^{*}Statistically significant.

TABLE 5 | Logistic regression analysis for factors associated with worse marital satisfaction.

Variable	Adjusted OR	95%	% CI	p value
		Lower	Upper	
Years of marriage	1.03	0.99	1.07	0.102
Education level				
Primary	12.67	1.40	114.87	0.024*
Secondary	11.52	1.39	95.72	0.024*
Tertiary	1.00			
FSFI Total Score	0.979	0.964	0.994	0.007*

 $[\]chi^2 = 32.662$, df = 5, p < 0.001; Nagelkerke $R^2 = 0.337$.

orgasm (24), or even premature menopausal symptoms (25). Chemotherapy may further impair patients' appearance with alopecia and weight loss (26), further contributing to sexual dysfunction. Likewise, radiotherapy may lead to vaginal stenosis and dyspareunia (27). Thus, sexual dysfunction can result in a substantial deleterious impact on marital relationships.

Education level has been demonstrated to be associated with female sexual dysfunction. In a large Iranian study involving 1,409 women in the general population, lower educational level was identified as a significant factor across different domains of sexual dysfunction including desire, arousal, orgasm, lubrication, and satisfaction with odds ratios ranging from 1.80 to 4.01 (28). Given the high likelihood of sexual dysfunction among gynecological cancer survivors (22, 23), it is probable that low education level also contributes considerably to poor adjustment of sexual function post-treatment, just as how it affects psychosocial adjustment in general among cancer survivors (9). For future interventions, the inclusion of patient's educational programs and relationship/couple therapy during rehabilitation programs is pivotal to enhance the couple's quality of marital relationship and subsequent sexual functioning among patients with gynecological cancer. Interestingly, studies have shown that a relationship between marital and sexual satisfaction may change over time. It is believed that the temporal association between these outcomes is dynamic rather than static (29). Moreover, patient education involving communications between patients and clinicians regarding sexual experience following treatment, alongside psychological interventions such as cognitive therapy, is important in improving the sexual wellbeing of the patients (30).

Studies have demonstrated previously that various demographic factors affect marital satisfaction. Such factors include age, number of children, length of the marriage, and educational attainment (31, 32). In this study, we did not find that age, the number of children, and length of marriage associate with marital satisfaction after controlling for confounders. It is interesting to note that in the study by Jose and Alfons among adults in the general population, education level was correlated with general-life adjustment problems and not sexual adjustment in the marital satisfaction questionnaire they used (Maudsley Marital Questionnaire, MMQ) (31). Specifically for women, there

is also conflicting but limited evidence regarding the relationship between education level and marital satisfaction. An earlier study found that women with more advanced education were more likely to experience unstable marriages (33). Contrarily, a population study in the United States concluded that more highly educated women had lower rates of marital dissolution (34). More research to study the influence of education level on marital satisfaction, especially among gynecologic cancer survivors, is thus needed.

Given that sexuality is an integral part of the quality of life, it is essential that health experts actively disclose information to women and their partners about the consequences of treatment in gynecologic cancers (35-38). It is crucial to authorize and normalize sexuality in this context of continuous consultation, for example, addressing their queries about their health and sexual-related matters during the routine consultation in the clinic. Future study in gynecologic cancer and sexuality demands researchers to address the pivotal role of bio-psycho-social interactions—how body and mind interact. For example, malaise due to the complication of radiotherapy causes low sexual desire, and low sexual desire may cause a lack of sexual satisfaction. This understanding and practice are often neglected in gynecological consultations with patients and healthcare workers (39). These include the physical/anatomical/material effects of disease treatments, sexual intimacy, psychodynamic factors, and their relationship with the partner. Shaping women's experiences and practices of sexuality post-gynecologic cancer can be a significant challenge to many clinicians.

This study had some limitations. Recruitment of study subjects by convenience sampling at a single site might limit the generalizability of its findings. However, as the study site is one of the few tertiary centers for gynecologic cancer treatment in the country, it is still quite representative of the Malaysian study population. As the study was cross-sectional in nature, the temporal relationship between studied variables, such as sexual dysfunction and marital dissatisfaction, could not be elucidated. Recall bias when answering the questionnaires was also possible.

In conclusion, both sexual dysfunction and education level are associated with marital satisfaction among gynecologic cancer survivors. Sexual dysfunction and low education level among gynecologic cancer survivors may independently affect their marital satisfaction. Given this, targeted efforts focusing on patients with low education levels and sexual dysfunction may help to improve their marital life.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Research Ethics Committee, National University

^{*}Statistically significant.

of Malaysia. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

SM and SH conceived and designed the study, reviewed and interpreted the results, and assisted in the writing of the manuscript. NN, SM, SH, and LW were involved in data collection. LW analyzed the data and wrote the main manuscript

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Speech After Long Silence—An Appraisee-Based Comprehensive Analysis With Retrospective and Future Perspectives on Current ID Policy of Transpersons in China

Jian Shi^{1,2}, Yadong Guo³, María José Cavagnaro⁴, Jifeng Cai³ and Zhuoying Liu^{5*}

¹ Department of Hematology and Critical Care Medicine, The Third Xiangya Hospital, Central South University, Changsha, China, ² Department of Spine Surgery, The Third Xiangya Hospital, Central South University, Changsha, China, ³ Department of Forensic Science, School of Basic Medical Sciences, Central South University, Changsha, China, ⁴ College of Medicine-Phoenix, University of Arizona, Phoenix, AZ, United States, ⁵ Health Law Research Center, School of Law, Central South University, Changsha, China

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*Correspondence:

Zhuoying Liu zhuoyingliu@csu.edu.cn

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Shi J, Guo Y, Cavagnaro MJ, Cai J and Liu Z (2021) Speech After Long Silence—An Appraisee-Based Comprehensive Analysis With Retrospective and Future Perspectives on Current ID Policy of Transpersons in China. Front. Public Health 9:793162. doi: 10.3389/fpubh.2021.793162 As the sexual minority in China, transpersons remain faced with various realistic challenges. In recent years, however, there has been a significant progress made in the protection given to the rights that transpersons deserve. Currently, the citizens who have changed their gender through sex reassignment surgery can make applications to the local police station for changing their gender registration and get issued a new ID card. This is regarded as a crucial milestone in reducing the bias against transpersons and protecting their legitimate rights in China. Highlighted by the case of an extraordinary appraisee who have received SRS to change from male to female and started a new life with a new ID, not only does this article construe the current ID policy and the detailed process of ID card change for transpersons in China, it also reveals the living and developmental conditions facing transpersons in China. Finally, the visibility of the community of transpersons is improved to eradicate the discrimination against transpersons.

Keywords: transpersons, public health, ID policy, psychosexual health, anti-transgender prejudice, health law

INTRODUCTION

Jin Xing, a Chinese transgender celebrity, once said "If the world is a sea, the heterosexual is a land, the homosexual is an island, but what I choose is a stone that can be placed on the land or the island, but neither of them belongs to me." ("I Can I BB" Qipa Shuo/Season 2, 20150711, iQIYI, Inc.). In China, the government takes a vague stance on lesbians, gays, bisexuals, transgender, and intersex (LGBTI). As one of the most populous countries around the world, China provides a significant base of the world's largest LGBTI community (1, 2). Despite a huge number of LGBTI in China (an estimate of 50–70 million population according to the seventh national population census of China), both state and local governments have chosen to distance themselves from those social issues in relation to sexual orientation and gender identity, holding a neutral attitude (3). The civil rights to which LGBTI people are entitled are exempt from protection in many parts of the country. For example, sex identification, marriage, kindred, employment, social welfare and

others (4–6). Up to now, LGBTI still suffer discrimination from those who consider it evil or contradictory to Chinese traditional culture, with transpersons in particular. In general, transgender can be classed into multiple categories. Besides, there is still no unified statement regarding the types of transsexuality in the academic circle. In this paper, our discussion is limited to those transpersons who have received sex-reassignment surgery (SRS).

Currently, there are some countries permitting their citizens to change their gender. Among them, Sweden took the lead in allowing people to change their legal gender identity in as early as 1972 (7). Since then, legal authorization has been increasingly expanded thanks to the bravery and dedication of social activists, which has prompted more and more other countries to follow suit in the formulation and enforcement of sex/gender identity recognition laws. The implications of the laws are made diverse and specific. For example, the United States, Italy, Japan, South Korea and Canada give recognition to the change in sex/gender in line with medical standards. In comparison, the United Kingdom, German, and Spanish Federal Constitutional Court jurisprudence apply the self-identity standards of recognition given to sex/gender change (8).

In China, transpersons encounter the toughest challenges, for example, they are subjected to unfair treatment and discrimination when their gender identity is made known to others (9). It is common for those male-to-female people to enter into such professions as sex workers, entertainers, and performers. The female-to-male community is deemed less acceptable (10). In addition, medical professionals often lack willingness to serve transpersons, who are left with limited access to medical care. Transpersons suffer discrimination and unfair treatment in medical facilities. Unexpectedly, more progress has been made in the protection of transsexual's rights than that of homosexuals, with the change in sex/gender identity receiving official recognition (11). As for the policies related to transpersons, in 2008, the Bureau of Public Security granted approval to household registration (known as Hu Kou in Chinese) after SRS. The citizens who have changed their gender identity through SRS can apply to the local police station for changing the gender registration, with the gender identification issued by the domestic tertiary hospital, the public certification issued by the notarial department, or the certification issued by judicial authentication institution. After approval is granted from the higher departments of the Bureau of Public Security, the local public security police station deals with gender-change registration through the formalities. The gender-change registration, with all the formalities gone through, can be completed in the police station of the seat of registered permanent residence rapidly. Then, the applicant would be issued the new ID cards and have updated household registrations.

It marks the first time that transpersons receive official recognition. Therefore, it is a legitimate right for Chinese transpersons to change their gender on ID cards and household registrations. In spite of this, it is still not the case that all transpersons going through full sex-reassignment surgery (SRS) are entitled to make the change. Notably, there are few successful cases of transpersons receiving a new ID since the

policy came into force. On the one hand, most people attach much importance to personal privacy. On the other hand, these social issues attract little attention from appraisal institutions. Therefore, there remain some questions needing to be answered. How has the policy actually been enforced in China? Can transpersons be successful in getting a new ID with a different gender identity after surgery? Fortunately, a case was collected from our cooperative appraisal institution, which is conducive to understanding the current state of transpersons. Let's take a look at the following case.

CASE PRESENTATION AND APPRAISAL OPINIONS

An appraisee, Xiao Ming (pseudonym), received SRS in September 2018 in Thailand. In order to change the gender identity as shown on household registration from male to female, Xiao Ming was given gender identification and offered judicial appraisal opinions in line with the rules set out by the Public Security Register Department. With approval granted by the local police department in charge of household registration, Xiao Ming hired an appraisal institution to carry out identification of her gender in March 2019. All the information presented in this study was collected from her and the cooperative appraisal institution.

Initially, Xiao Ming made application to an appraisal institution, along with three notarial certificates received from the notary offices. Notarization affairs: the translation of the medical record in the Thai language. The medical certificate was issued by a hospital in Thailand, the purpose of which is to certify that Xiao Ming has received a sex reassignment surgery performed by a registered doctor.

Examination results: there was no evidence suggesting psychosis. Diagnosis: gender anxiety disorder and gender identity disorder. Changing from male to female, Xiao Ming received SRS in Thailand. Besides, Xiao Ming received the surgeries purposed to reduce laryngeal prominence and correct breast. These operations were completed smoothly. Currently, the health condition is stable. Then, the appraiser carried out forensic examination on Xiao Ming, which confirmed that the appraisee was generally healthy. The appraisee was fully conscious and dressed as a female. Physical examination: no beard on the upper lip, no distinctive laryngeal prominence on the neck. With double plump female breasts, arc operation scars are visible at the bottom edge of double breasts. Perineal examination: no penile or scrotal structures. Labium majus, minus, and vagina can be seen after resetting surgery. The analysis and description of the appraisal constitution are detailed as follows:

 According to the regulations published by the public security administration bureau of public security in 2008, "approval and reply of issues related to the project of gender-change in citizen's household registration after undergoing SRS," the acceptance of such kind of cases by the judicial appraisal institution is compliant with the applicable national regulations.

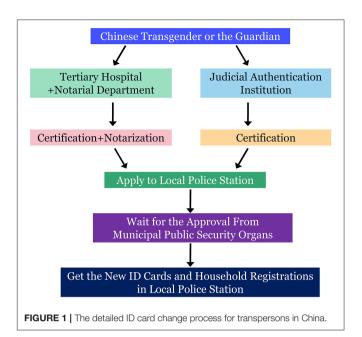
- According to the data sourced from the entrusting party, it
 is reaffirmed that Xiaoming was a male and has undergone
 the SRS, from male to female. A forensic examination
 was conducted to identify the female secondary sexual
 characteristics, including female breast, labium majus, minus,
 and vagina.
- 3. For humans, their gender identity can be classified into genetic gender, chromosomal gender, gonadal gender, genital gender, and psychological gender. The identification of gender is associated with the gender role played in a specific living environment. Gender is frequently transferred and consolidated not only in the social system but also in the course of individual socialization, which reflects a gender relationship that is acquired and changeable.

The definitive appraisal opinions: Xiao Ming received the male-to-female SRS under no restrictive operation conditions. Currently, Xiao Ming is female. Finally, Xiao Ming submitted the appraisal opinions to the local police department of household registration, which led to a success in changing the gender identity shown on her household registration from male to female. Eventually, she was issued a new ID card. In this circumstance, the appraisal institution gave recognition to the female gender of Xiao Ming, given her psychological gender and genital gender. It was also recognized that gender could be transferred and consolidated through individual socialization. Most importantly, it demonstrated that the Chinese government has put in place a policy aimed to support those transpersons who have received SRS to start a new life with a new ID.

DISCUSSION

People are entitled to choose their own gender. What is inspiring is the legal recognition given to this. To the best of our knowledge, there have been a number of similar judicial appraisals made in China over recent years. Eventually, all appraises were granted the corresponding gender identification. Once the identification is issued by the judicial authentication department, transpersons can go through the gender-changing procedures with the police station in an instant, before getting granted new citizenship and having the same rights as other Chinese citizens do. Notably, the public security departments routinely recommend the permission of the judicial authentication department instead of the hospital. Moreover, all of the applicants change from male to female. However, the femaleto-male transpersons may be reluctant to come under such public pressure.

At present, there are still limited precise statistics about transsexuals in China. Firstly, a large proportion of transpersons are unwilling to have exposure to the public and they may choose to live abroad. Secondly, the mainstream media in China refrains from covering such news. Moreover, it is practically difficult to calculate the percentage of transgender population, which is attributed in part to the unified concept of transpersons.



Despite a huge number of LGBTI in China, the process of protecting their rights through legislation remains at a very slow pace. In contrast, the social attitude toward LGBTI has improved in recent years. To a large extent, this is attributable to the efforts put in by many organizations and individuals over the years. As for the LGBTI civil engagement with a sense of mission, there has been remarkable achievements made in protecting the rights of homosexuals in China from various perspectives including law, policy, social and cultural attitude, etc. (11). In 2008, the policies aimed for household registration specifically involving transpersons after SRS were published by the Bureau of Public Security, which marks a key milestone in allowing those transpersons who received SRS to get a new ID card for starting a new life. The ID-changing process is detailed in **Figure 1**.

As a matter of fact, Chinese hospitals have no problem at all with performing SRS. However, there remain plenty of transpersons preferring Thailand or other countries for doing it, which is largely attributed to the complex procedures in China. For example, the requirements for surgery lasted for a minimum of 5 years without hesitation. It is a difficult period for transpersons who are keen on receiving SRS. Moreover, the psychological and psychiatric treatment carried out before the operation lasts at least 1 year. The applicants are required to be 18 or over and have received consent from their relatives with lineal consanguinity. Apart from that, there are many other rigid requirements. It is expected that, our Chinese policies will be made more considerate for transpersons in the future. Furthermore, marriage is possibly the most prominent right needing protection. So far, there are only a handful of countries or states around the world where recognition is given to samesex marriage (12). Professor Yinhe Li, who is a researcher of the Chinese Academy of Social Sciences, is among the advocates for legalizing same-sex marriage. According to Li, there was a case occurring in 1997 when a gay soldier got caught having sex with another man and arrested as a rogue. After being detained, he received a certificate from the hospital stating that he was mentally ill. For this reason, homosexuality was not classified as a psychological anomaly until after 2001. "2001 was a turning point when there was the first-ever positive coverage of China's LGBTI community in the official media. After that, all official media outlets, whether paper, TV or online, started mentioning the LGBTI community a lot more." With the elapse of nearly two decades, however, there remains a long way to go for the legalization of same-sex marriage in China. It is thus concluded that transgender marriage is less likely to be legally recognized. In spite of the little progress at present in China toward removing the discrimination and prejudice on transpersons, we found that transpersons with new identities have become more confident and happy in life in our limited interviews on Chinese transpersons for whom the SRS was performed. In the past, many transpersons in China were very nervous talking about their true sexual identities. But nowadays, more people are open and ready to let others know about them and fight for their rights. The current ID policy of transpersons, to some extent, is really making changes to a relatively inactive social environment. Meanwhile, it's important to praise equal rights between male and female, sexual majority and sexual minority, and revise the policy more inclusive and equal. The entitlements for transpersons are also very important like the gender affirmative ID and individualized medical security project.

Jin Xing has honestly chosen to be herself and active on the screen with her commendable personal abilities, without nothing concealed, which makes it inevitable for her to be targeted by some vicious cyber-violence. On the contrary, respect, and admiration are received from the audience. It is extremely tough to resolutely choose to be yourself when realizing that you are "not gregarious." Finally, she responded by saying, "This stone is my choice, without anyone forcing me, and I want to stand on

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

AUTHOR CONTRIBUTIONS

citizens standing on the land.

ZL and JS: conceptualization, formal analysis, writing–original draft, and writing-review and editing. JC: conceptualization, formal analysis, writing–review and editing, funding acquisition, and project administration. MC and YG: writing-final draft and methodology. All authors contributed to the article and approved the submitted version.

that stone." ("I Can I BB" Qipa Shuo/Season 2, 20150711, iQIYI,

Inc.). When the legal system in China improves constantly, there

are more people who will feel safe after making attempt to

maintain a balance on the stone. Moreover, those standing on

the stone or the island can enjoy the same rights as their fellow

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Quality of Life, Sexual Health, and Associated Factors Among the Sexually Active Adults in a Metro City of India: An Inquiry During the COVID-19 Pandemic-Related Lockdown

Seshadri Sekhar Chatterjee¹, Ranjan Bhattacharyya², Amrita Chakraborty¹, Arista Lahiri^{3*} and Abhijit Dasgupta⁴

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*Correspondence:

Arista Lahiri alahiri@bcrmrc.iitkgp.ac.in

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¹ Department of Psychiatry, Diamond Harbour Government Medical College and Hospital, Diamond Harbour, India,

² Department of Psychiatry, Murshidabad Medical College and Hospital, Berhampore, India, ³ Dr. B. C. Roy Multi-Speciality Medical Research Centre, Indian Institute of Technology Kharagpur, Kharagpur, India, ⁴ Department of Medicine, University College Dublin, Dublin, Ireland

Background: Sexual dysfunction (SD) and its effect on our life is an important but less studied topic especially during post-COVID era. This study examines the extent of SD and other mental health predictors and their effect on quality of life.

Methods: A cross-sectional survey of sexually active adults was conducted in an Indian metro-city. Along with sociodemographic data, sexual dysfunction, depression, anxiety, stress, and quality of life were assessed by Arizona Sexual Experience Scale (ASEX), Depression Anxiety and Stress Scale (DASS), and WHOQOL-BREF, respectively. Structural equations modeling was used to understand their relationship.

Results: Out of the total 1,376 respondents, 80.52% were male, 65.98% were married, and 48.54% were graduates. The mean age of the participants was 34.42 (\pm 9.34) years. Of the participants, 27.18% had sexual dysfunction. Majority of the respondents did not have depression (59.30%), anxiety (52.33%), or stress (44.48%). Mild and moderate levels were the commonest findings among those who had depression, anxiety, or stress. Among the respondents, 27.18% had sexual dysfunction as per the ASEX instrument. Increase in age and female gender were associated with sexual dysfunction overall and also all its components. Presence of depression adversely affected ease of achieving orgasm and satisfaction from orgasm and was associated with sexual dysfunction overall. The respondents had a mean score of 73.57 (\pm 13.50) as per the WHO-QOL. Depression and stress emerged as statistically significant factors for poor quality of life, while sexual dysfunction was not associated statistically.

Conclusion: More than one-fourth of the study population reported sexual dysfunction during the first wave of the pandemic in India. The study findings highlight the role of

poor mental health issues in this regard. In fact, issues like depression and stress were associated with poor quality of life as well. The current findings unequivocally warrant specific interventions to improve mental health of the respondents.

Keywords: sexual dysfunction, anxiety, depression, stress, psychosexual, survey, pandemic, quality of life

INTRODUCTION

Sexual wellbeing is essential for maintaining overall physical and mental health through a variety of biological and psychological processes (1–3). Regular sexual activity reduces stress, regularizes sleep cycle, and regulates our mental wellbeing as a whole. On the contrary, the persistent depression and anxiety can affect sexual health (SH), which in turn lowers our quality of life (4). Following the coronavirus disease 2019 (COVID-19) spread, complete lockdown for a long time, new social norms, quarantine- and isolation-related issue, and even unpredictable geopolitical situations has affected the lives of the citizens (5). Several mental-health-related issues were identified in India during the lockdown period (6). Physical distancing, lack of peer group interaction, isolation during incubation days, "touch hunger," and relationship problems all can directly or indirectly affect SH.

Mental health significantly influences sexual behavior, including sexual intercourse frequency. Generally, perceived wellbeing and mental health are positively associated with sexual pleasure and intercourse. Sometimes people with stress might get engaged in excessive sexual activity to reduce their stress levels. Alternatively, excessive worry and decreased motivation because of stress can also reduce sexual interest, arousal, and intercourse frequency (7). A scoping review on SH (excluding reproductive health, intimate partner violence, and gender-based violence) and COVID-19 by Kumar et al. finds very few studies done on the same subjects in low-/middle-income countries (LMICs) (8). SH has been neglected during any disaster, as other, more basic issues like primary medical care, safety, and nutrition become the priority (9). Any disasters will impair SH, which can be due to poor access to SH services and supplies, disrupted health facilities, reduced human resources, impoverishment, and exposure to sexual violence (10).

The past works reporting the investment in SH services following disasters are low leading to higher unmet needs (11). Although there are some studies already conducted on sexual health, only few empirical studies have focused on the associated factors. Studies done among various physiological and demographic groups during the pandemic have highlighted the role of depressive symptoms, anxiety, stress, and clinicobehaviors including addictions for being associated with SH (12-17). Often, sexual and mental health issues have been studied together (18). The existing literature, both during and before the pandemic, informs the importance of depression, anxiety, stress, different comorbidities, addiction habits like smoking, and social norms like marriage, etc. in the backdrop of age and gender, for understanding SH and the emergence or severity of sexual dysfunction (SD). The evidence in Indian context is even lesser, which brings forward the need for understanding the role of these factors, which are essentially modifiable in sexual dysfunction among the adult sexually active participants.

SD alone and also in synchrony with mental health conditions, physical ill health, and addictions impacts the overall quality of life of an individual (19-22). Researchers have explored the continuum of mental health, sexual dysfunction, and quality of life using path analysis as well (21). However, this continuum is not well explored amidst the COVID-19 pandemic. In addition, the role of practice of COVID-appropriate behaviors, economic loss, loss of job during lockdown, etc. appear to be plausible factors leading to a poor quality of life. Thus, not only the contributors of SD but also their role in synergy with SD, and different socio-behavioral factors' role on quality of life are important contemporary considerations. The most useful analytical technique in this regard to study this continuum and explore the effect sizes for different contributors, also taking into account the endogeneity of SD in the continuum path, is structural equations modeling (SEM) (23-25). In this backdrop, the present study was conducted to measure the proportion of sexual dysfunction among the study population and determine its association with different psychiatric morbidities. This article also explored the association of sexual dysfunction with quality of life of the participants.

METHODS

Study Design and Participants

A cross-sectional study was carried out among the adult population aged 18 years and above residing in a Metropolitan city of Eastern India (Kolkata). Following approval from the Institutional Ethics Committee, an online questionnaire was distributed, with a digital consent form attached to it. Study population consisted of adults. Only those who provided consent could access the questionnaire. Those who ultimately completed the whole questionnaire were included. Eligible respondents but with known pre-existing psychiatric morbidity or on regular medication for any psychiatric or sexual problems were excluded from the study through skip questions.

The data collection for the study was conducted over a period of 1 month during the gradual easing off of the lockdown restrictions by the Government of India, from July 28, 2020, 12:00 h to August 29, 2020, 23:59 h. The sample size for this study was calculated based on the proportion of sexual dysfunction from a pilot study conducted beforehand. Based on the proportion of 14.40%, with 90% power of the study and 5% precision, with a design effect of 2, the minimum required sample size was noted to be 1,365. From the location data of social media users (Facebook, Twitter, LinkedIn, and Instagram), a list of respondents residing in greater Kolkata region was prepared. From this list, considering 10%

non-response, 1,500 participants were shared the questionnaire digitally. Ultimately, a total of 1,376 completed responses were obtained and analyzed.

Tools and Measurements

The study tool was a pre-designed, pre-tested validated questionnaire with four sections prepared in the English language. The Section Introduction consisted of socio-demographic characteristics like age, gender, education, occupation, and income. It also comprised questions on comorbidities, smoking habits, and practice of COVID-appropriate behaviors. Section Methods assessed mental health status of the participants in terms of depression, anxiety, and stress with the help of the DASS21 questionnaire (26). Section Results was about the questions on sexual health, which was assessed using the Arizona Sexual Experience Scale (ASEX). In Section Discussion, the WHOQOL-BREF scale was used to assess the quality of life (27).

Depression Anxiety Stress Scale (DASS)

The 21-item DASS tool (DASS-21) measured depression, anxiety, and stressed with its subscales, each comprising seven items. Response to each item was noted on a 4-point Likert scale from 0 to 3, with a higher score indicating depression or anxiety or stress as per the respective subscale corresponding to the items. In the current sample, Cronbach's alpha values were found to be 0.88 for stress subscale, 0.79 for anxiety, and 0.83 for depression subscales. For each subscale, the respective itemspecific scores were summated, and then, resultant scores were doubled. Depression, anxiety, and stress as per this instrument were classified in five resulting categories, i.e., normal (total score: 0-9 for depression, 0-7 for anxiety, and 0-14 for stress subscales), mild (total score: 10-13 for depression, 8-9 for anxiety, and 15-18 for stress subscales), moderate (total score: 14-20 for depression, 10-14 for anxiety, and 19-25 for stress subscales), severe (total score: 21-27 for depression, 15-19 for anxiety, and 26–33 for stress subscales), and extremely severe (total score \geq 28 for depression, >20 for anxiety, and >34 for stress subscales, respectively) (26).

Arizona Sexual Experience Scale (ASEX Scale)

ASEX is a five-item self-report inventory, with each item measured on a 6-point Likert scale. Sexual function in men and women were measured regardless of their sexual orientation or relationship with a partner. It measured the quality of sexual functioning in terms of five questions, with each question representing one domain, i.e., sexual drive, arousal, penile erection/vaginal lubrication, ability to reach orgasm, and satisfaction from orgasm. The scores in each of the items were aggregated. Clinical sexual dysfunction was identified if a total score of >19 was observed, and/or in any one item score was >5, and/or in any three items, a score of >4 was noted (28). The Cronbach's alpha value for ASEX in the study sample was 0.83.

WHO Quality of Life Questionnaire (WHOQOL-BREF)

The WHOQOL-BREF instrument comprises 26 items, which measure the following broad domains: physical health, psychological health, social relationships, and environment.

In each domain, the domain-specific item scores are summed up to denote the domain-specific score. This domain-specific score is a measure of quality of life in that particular domain only. The overall quality of life is measured by summing up all the item-specific scores. The higher the score, the better is the quality of life in any domain or overall (27). The overall Cronbach's alpha value for WHOQOL-BREF was observed to be 0.91, with the alpha value for the subscales ranging between 0.85 and 0.93.

Statistical Analysis

The statistical analysis was conducted in STATA 14.2 (StataCorp., College Station, TX, USA). Considering the variables of interest, the Generalized Structural Equations Model (GSEM) was utilized to analyze the relationships between the variables. The main GSEM predicted the WHOQOL-BREF total score in terms of sexual dysfunction, depression, anxiety, stress, and other clinical and behavioral variables. In the same model, sexual dysfunction was in turn predicted by depression, anxiety, stress, and selected clinical and behavioral factors. On the other hand, five separate GSEMs were developed to predict each component of sexual dysfunction. In each of these models, the major predictors were depression, anxiety, and stress and also other clinical and behavioral factors. Depression, anxiety, and stress each were predicted by socio-demographic and behavioral factors. The categorical variables with ordinal measurements, e.g., depression, anxiety, stress, loss of income during lockdown (in comparative percentage), and income ranges, were incorporated in the models using probit link. The variables with nominal measurements (e.g., education, marital status, etc.) and the dichotomous variables logit links were used. Age was taken as a continuous variable with identity link. Coefficient (Coef.) with 95% confidence interval (95% CI) has been considered as the measurement of effect. The main effects, i.e., effect of the major predictors on different outcomes (i.e., quality of life, sexual dysfunction and its components), are presented in the results section, along with the reference categories for the predictor variables in these models.

RESULTS

Background Characteristics

Table 1 summarizes the socio-demographic background of the participants. Out of the total 1,376 respondents, 80.52% were male, 65.98% were married, 48.54% were graduates, while majority had been working in private companies (42.73%). The mean age of the participants was 34.42 (±9.34) years. Majority (61.63%) of the respondents belonged to the age group of 19–35 years. Among the respondents, 10.76% had lost their jobs during the lockdown. While majority (41.86%) reported that their monthly family income did not decrease during the lockdown, 17.15%, on the other hand, reported that their incomes decreased by more than half of their pre-lockdown income. However, 36.63% of the respondents had a monthly family income of >50,000 Rupees per month.

Clinical and Behavioral Profile of the Participants

Table 2 shows the clinical and behavioral characteristics of the study participants. Majority (79.02%) did not report

TABLE 1 | Background characteristics of the study participants.

Background characteristics	N	%
Age	[3	34.42 (±9.34) years]
19-35 years	848	61.63
36-50 years	460	33.43
51-65 years	56	4.07
>65 years	12	0.87
Gender		
Male	1,108	80.52
Female	268	19.48
Marital status		
Unmarried	417	30.31
Married	908	65.99
Separated	28	2.03
Divorced	16	1.16
Widow	7	0.51
Education		
Secondary level	16	1.16
Higher-secondary level	84	6.10
Graduation level	680	49.42
Post-graduation level	596	43.31
Occupation		
Laborer	24	1.74
Businessman	132	9.59
Government sector employees	256	18.60
Private sector employees	588	42.73
Professionals	68	4.94
Other	308	22.38
Monthly family income (in Rupees)		
≤3,000	84	6.10
3,001-10,000	140	10.17
10,001–25,000	272	19.77
25,001–50,000	376	27.33
>50,000	504	36.63
Loss of monthly income during lockd	own	
No change	576	41.86
≤10%	168	12.21
11–25%	212	15.41
26–50%	184	13.37
>50%	236	17.15

N, number of respondents; %, percentage of respondents in each category.

any comorbidities. However, some had diabetes (10.47%), some had pulmonary comorbidities (9.59%), and few of the respondents had diagnosed chronic kidney disease (1.74%). Majority of the respondents did not have depression (59.30%), anxiety (52.33%), or stress (44.48%). Mild and moderate levels were the most common findings among those who had depression, anxiety, or stress. Regarding maintaining COVID-19 appropriate behaviors, most of the participants were observing the recommended norms.

Sexual Dysfunction and Its Associated Factors

Among the respondents, 27.18% had sexual dysfunction as per the ASEX instrument. The item-wise responses of ASEX are

TABLE 2 | Clinical and behavioral profile of the respondents.

Clinical and behavioral factors	N	%
Known comorbidities*		
Diabetes	144	10.47
Asthma/COPD	132	9.59
Chronic kidney disease	24	1.74
Smoking history		
Presently a smoker	616	44.77
Not a smoker	760	55.23
COVID-19 preventive behaviors*		
Regular use of masks	1,352	98.30
Maintaining physical distancing	1,103	80.20
Regular hand wash by soap and water and/or use of sanitizer	1,252	91.00
Maintaining cough hygiene	1,348	98.00
Regular examination with thermal scanner	364	26.50
Depression		
Normal	816	59.30
Mild	192	13.95
Moderate	188	13.66
Severe	88	6.40
Extremely severe	92	6.69
Anxiety		
Normal	720	52.33
Mild	184	13.37
Moderate	308	22.38
Severe	76	5.52
Extremely severe	88	6.40
Stress		
Normal	612	44.48
Mild	488	35.47
Moderate	140	10.17
Severe	100	7.27
Extremely severe	36	2.62

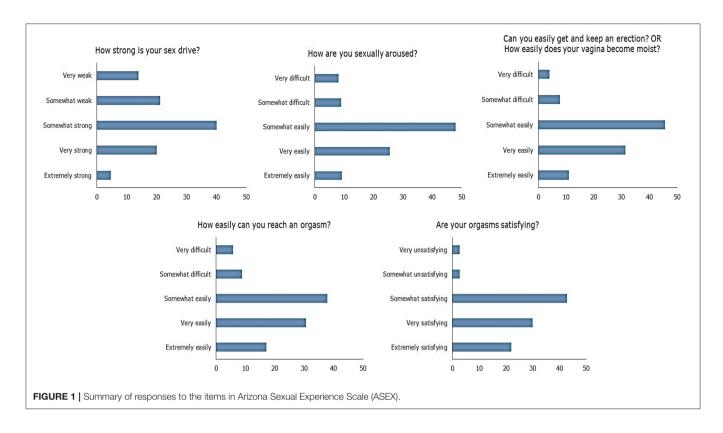
N, number of respondents; %, percentage of respondents in each category; COPD, chronic obstructive pulmonary disease.

depicted in Figure 1. Table 3 summarizes the key associations in terms of the components of ASEX and also overall sexual dysfunction from five separate GSEMs and the main GSEM, respectively. The relationships of socio-demographic and clinical factors with the components of ASEX and also with overall presence of sexual dysfunction are depicted. Increase in age and female gender were associated with sexual dysfunction overall, and also with all its components independently. The presence of depression adversely affected ease of achieving orgasm and satisfaction from orgasm. Depression was overall statistically associated with sexual dysfunction among the respondents. In addition, the presence of any comorbidity was associated with sexual dysfunction.

Association of Sexual Dysfunction With Quality of Life of the Respondents

Regarding quality of life, the respondents had a mean score of 73.57 (\pm 13.50). **Table 4** depicts the results of GSEM analysis

^{*}Multiple response.



showing association between the quality-of-life score with sexual dysfunction, adjusted for other relevant variables. Sexual dysfunction was not observed to be statistically associated with quality of life among the respondents. However, depression and stress with the exception of anxiety emerged as statistically significant factors for poor quality of life among the respondents. Maintaining a COVID-19 preventive behavior was also not statistically associated with quality-of-life score.

DISCUSSION

Findings in Light of Existing Literature Comorbidities in the Case of Sexual Dysfunction

In a sample of 1,376 individuals residing in Kolkata, 27% had SD as per ASEX scoring criteria. A pre-COVID-19 era epidemiological study conducted in a South Indian population using the same scale (ASEX) reported its prevalence to be 21% (male) and 15% (female) (29). The psychometric construct of ASEX typically considers high scores to demarcate SD. However, it was proposed by the makers of ASEX to consider subjects having premature ejaculation or spontaneous orgasm (reflected in extremely low ASEX scores) to have sexual dysfunction, given that sexual dysfunction can involve both hyperfunction and hypofunction (28). Older men, diabetic male patients, men with cardiovascular disease, men who are overweight/obesity, and those with multiple comorbidities are at highest risk for suffering serious complications secondary to COVID-19, and they are also at risk for erectile dysfunction (ED), which is the most common sexual health concern among men (30). ED is an excellent surrogate marker of systemic health, in general, and vascular performance, in particular (endothelial dysfunction resulting in erectile dysfunction and vice versa) (31).

Approximately 20% of the respondents suffered from chronic health issues: diabetes (10.5%), COPD and asthma (9.6%), and hypertension, which exemplifies the emergence of noncommunicable diseases, especially diabetes, in recent times. This finding in a population who are predominantly young is a grim reminder of the warning that India is the new diabetes capital of world (32). The finding that almost all are following COVID protocol is encouraging, yet subjected to possible conformity and response bias as observed by prior epidemiological studies (33). No statistical relation was found between sexual dysfunction and maintaining COVID protocol: sexual abstinence owing to fear of infection and non-compliance to precautionary measure resulting from sexual frustration are enlisted by Banerjee in the "Probable sexuality and intimacyrelated issues during pandemic" (34). There are not enough data to comment on the first concern, but the presence of the latter issue is not established with the study population.

The Role of Depression, Anxiety, and Stress

The prevalence of some level of depression was \sim 40% in the study population (12% were suffering from severe and very severe depression), whereas almost half of the population (47%) were experiencing some level of anxiety. This finding is similar to the earlier works carried out in India (35, 36). Recent meta-analysis found that one-third of the population are suffering from depression and anxiety (37). Among the population, this

TABLE 3 | Generalized structural equations model analysis showing relationship of socio-demographic and clinical factors with sexual dysfunction among the respondents.

	Desire		Excitement		Erection/lubrication	ion	Orgasm		Orgasmic satisfaction	action	Overall sexual dysfunction	function
	Coef. (95% CI) p-value Coef. (95% of	p-value	ਰ	p-value	Coef. (95% CI)	p-value	Coef. (95% CI)	p-value	Coef. (95% CI)	p-value	Coef. (95% CI)	p-value
Depression ^a	0.09 (-0.03, 0.22) 0.138	0.138	0.13 (-0.01, 0.26)	0.075	0.19 (0.06, 0.32)	0.003	0.45 (0.19, 0.71)	0.001	0.58 (0.35, 0.81)	0.000	0.30 (0.14, 0.46)	0.000
Anxiety ^a	-0.10 (0.23, 0.03)	0.146	-0.10 (-0.22, 0.02)	0.100	-0.10 (-0.21, 0.01)	0.071	0.04 (-0.17, 0.26)	0.689	0.28 (0.09, 0.47)	0.005	0.02 (-0.14, 0.17)	0.834
Stress ^a	0.13 (-0.03, 0.29)	0.113	0.07 (-0.10, 0.24)	0.399	0.05 (-0.12, 0.22)	0.549	-0.05 (-0.31, 0.22)	0.727	0.07 (-0.21, 0.34)	0.636	-0.03 (-0.24, 0.18)	0.783
Ageb	0.05 (0.04, 0.06)	0.000	0.04 (0.02, 0.05)	0.000	0.04 (0.03, 0.06)	0.000	0.04 (0.02, 0.06)	0.001	0.04 (0.02, 0.06)	0.000	0.05 (0.03, 0.06)	0.000
Sex	0.42 (0.13, 0.71)	0.004	0.94 (0.61, 1.26)	0.000	1.33 (1.03, 1.63)	0.000	2.07 (1.64, 2.50)	0.000	0.83 (0.36, 1.31)	0.001	0.87 (0.51, 1.23)	0.000
Marital status ^d	-0.55 (-0.79, -0.32)	0.000	-0.58 (-0.84, -0.32)	0.000	-0.39 (-0.67, -0.12)	0.005	-0.19 (-0.72, 0.33)	0.472	0.00 (-0.58, 0.58)	0.996	-0.28 (-0.61, 0.05)	960.0
Presence of comorbidities ^c	0.16 (-0.11, 0.43)	0.244	0.25 (-0.05, 0.55)	0.103	0.53 (0.22, 0.84)	0.001	0.24 (-0.12, 0.59)	0.188	0.32 (-0.08, 0.71)	0.122	0.43 (0.13, 0.73)	0.005
Smoking status ^c	0.19 (-0.03, 0.40)	0.094	0.19 (-0.03, 0.40) 0.094 -0.05 (-0.28, 0.18) 0.679	0.679	-0.24 (-0.47, -0.01) 0.040 -0.17 (-0.48, 0.13) 0.267 -0.25 (-0.56, 0.06) 0.120	0.040	-0.17 (-0.48, 0.13)	0.267	-0.25 (-0.56, 0.06)	0.120	-0.22 (-0.50, 0.06)	0.120

Coef., coefficient of regression equations; CI, confidence interval.

Probit linkage used for ordinal level of measurement for these variables with assumption of homogeneity of risk. The reference categories for Depression, Anxiety, and Stress are the "Normal" groups.

and smoking status the reference categories were "absence of any comorbidity" and "nonthe reference category, while in the case of presence of comorbidities, ²Age was taken in a continuous scale of measurement assuming Gaussian distribution and using identity linkage

F0, and previously married. currently married, unmarried, ViΣ., yielding three nominal level married" 'previously and the coefficient was calculated taking the "Unmarried" into categories The bold values indicate statistically significant. status, Divorced,

this variable,

TABLE 4 | Relationship between socio-clinical factors and quality-of-life of the respondents as per generalized structural equations model analysis.

Variables	Coef. (95% CI) for a higher QOL score	p-value
Depression ^b	-3.92 (-4.61, -3.24)	0.000
Anxiety ^b	0.18 (-0.51, 0.88)	0.606
Stress ^b	-3.01 (-3.99, -2.04)	0.000
Age ^c	0.03 (-0.06, 0.11)	0.550
Sex ^a	1.20 (-0.37, 2.78)	0.135
Marital status ^d	1.12 (-0.32, 2.56)	0.127
Income loss ^b	-0.93 (-1.36, -0.50)	0.000
Lost job ^a	5.71 (3.72, 7.69)	0.000
Maintaining COVID protocola	-1.10 (-2.69, 0.49)	0.174
Presence of any comorbidity ^a	-2.81 (-4.36, -1.27)	0.000
Monthly family income ^b	0.43 (-0.09, 0.94)	0.107
Smoking status ^a	1.10 (-0.10, 2.29)	0.071
Educational levele	-0.66 (-1.55, 0.24)	0.150

Coef., coefficient of regression equations; CI, confidence interval; QOL, quality of life.
^aThese variables were measured dichotomously. For sex, "male" was the reference category, while in the case of lost job, presence of comorbidities, and smoking status, the reference categories were "did not lose job," "absence of any comorbidity," and "non-smoker," respectively. "No sexual dysfunction' was the reference category for sexual dysfunction.

^b Probit linkage used for ordinal level of measurement for these variables with assumption of homogeneity of risk. The reference categories for Depression, Anxiety, Stress are the "Normal" groups. For Monthly family income and Income loss, the reference categories were, "≤3,000 Rupees per month" and "No Change," respectively.

^cAge was taken in a continuous scale of measurement assuming Gaussian distribution and using identity linkage.

dFor marital status, Divorced, Separated, and Widow categories were merged into "previously married" category yielding three nominal level categories, viz., unmarried, currently married, and previously married. For this variable, also uniformity of risk was assumed, and the coefficient was calculated taking "Unmarried" group as reference.

^eSecondary and higher-secondary categories were combined into "below graduation" category, which was the reference category.

The bold values indicate statistically significant.

result, which surfaced in a screening survey, warrant us about the treatment gap in mental illness in India, which is as high as 80%, and this is bound to increase further in post-COVID scenario (38).

The current study found that people suffering from depression have more chance of having sexual dysfunction. The findings are in consonance with the current literature. While a Polish study established the correlation of depression and SD in women, in the study by Fang et al., this association was established among the men (15, 17). Both behavioral and biological models have been proposed to explain this relationship. The behavioral model postulates that patients with depression tend to engage in negative thought and are less confident, which results in performance anxiety that further reduces erectile function, whereas the biological model postulates that depression affects the hypothalamic–pituitary–adrenocortical (HPA) axis, leading to excess catecholamine production, which in turn leads to poor cavernosal muscle relaxation and ED.

Anxiety and stress were not found to be significantly associated with SD in the present study. Culha et al. in this regard

found out that during the pandemic, anxiety was associated with SD but not depression or stress (13). On the other hand, in a study from China, anxiety was correlated with SD in men (15). It is easier to blame COVID-related stress for poor sexual health, but the relationship between the two is complex. Increased levels of stress can reduce sexual urge, but social distancing and stressful circumstances can also increase the need for emotional bonding. Online communication as a form of prosocial behavior at the time of a stressful event can encourage and strengthen people's bonds. Regardless of one's relationship status, expressing intimacy is vital to sustaining positive coping and psychological wellbeing. It is interesting to observe a paradoxical increase in pornography consumption globally during peak of pandemic. As reported, worldwide traffic to pornographic websites skyrocketed compared to the situation before the pandemic during the month of February and March 2020 when Europe was under full lockdown (39). The "Dual Control Model of Sexual Response" theory might be a plausible explanation to the contradictory and paradoxical relationship between stress and sexuality. From this lens, people who tend to be sexually inhibited would have a more difficult time becoming aroused in stressful situations, whereas times of anxiety and stress may amplify sexual arousal in people who are usually easily excitable (30).

Association of Age and Gender

Female gender appeared as a significant correlate of SD in the present study. This supports the finding by other researchers that sexual problems are much under-reported among women (40). Desire, arousal, erection, and orgasm difficulties, all these are significantly predicted by female gender and being ever married. Among other authors who studied sexual behavior during COVID pandemic, few studies indicated reduction in sexual function in women and an increase in female sexual dysfunction in general (41, 42). Other researchers, in contrast, noted that during the pandemic, despite a sharp decrease in the quality of sexual life in women, sexual desire and frequency of intercourse significantly increased (43). However, in a study during the pandemic in Turkey among healthcare workers, male gender was identified as a significant factor for sexual dysfunction (13). This contrast may again be attributed to a probable underreporting of SH status of women.

A common disorder in the spectrum of female sexual dysfunction (FSD) is decreased vaginal lubrication (which is deemed equivalent to erection phase in men) during the COVID-19 pandemic, which in turn leads to other problems, such as dyspareunia, orgasm dysfunction, vagina irritation, or increased risk of vaginitis (44). From a traditional outlook, "lockdown" for a man provided longer time to interact with the spouse, but for most women, it meant an increase in the workload in all spheres (domestic, working from home professionally, and looking after children attending online classes). Ironically, when one partner is looking to have more sex and the other is distracted, preoccupied, or otherwise disengaged, the issue of sexual desire discrepancies arises (18). Additionally, the presence of everyone at home throughout the day combined with higher work pressure led to frequent interpersonal issues and more chances of domestic violence (45). Interestingly, the smallest decline in sexual activity was noted in women who were working outside the home (44). Pre-pandemic research involving ASEX to identify sexual dysfunction in patients of the schizophrenia spectrum found a much higher rate in women (79.2%) than in men (33.3%). Indeed, women reported high frequencies of sexual dysfunctions in all stages of sexual activities (sexual drive, arousal, vaginal lubrification, ability to reach orgasm, and satisfaction with orgasm) (46). This difference between genders can be attributed to biopsychosocial factors: sexual hormones (estrogens vs. androgens), sexual education (repressing vs. permissive), and environment (controlling vs. stimulant) (47).

Increasing age emerged as a significant predictor of difficulties in all spheres of sexual cycle (desire, arousal, erection, and orgasm). To elaborate the association of increasing age with SD, prior authors mentioned that sexual dysfunction worsens with age. Thirty-nine percent of 40-year-olds have some degree of erectile dysfunction (5% are completely impotent), but by the age of 70, two-thirds have some degree of erectile dysfunction and complete impotence triples to 15% (48). Occurrence of SD with increasing age might be explained by poorer vascular health and endothelial dysfunction as explained earlier.

The Issue of Quality of Life

In our study, SD was not statistically associated with quality of life (QoL). The association of QoL with ED studied earlier mostly showed deleterious effect of ED on life satisfaction and overall QoL. Rosen, on the other hand, suggested an indirect pathway model that hypothesized that changes in erectile function (EF) through treatment were associated with improved mood and quality of sexual life, which resulted in improved partner satisfaction, family life, and overall life satisfaction. These data suggest that QoL changes associated with ED therapy may be mediated by changes in sexual function, mood, and family relationships (21). UK-based survey demonstrated that men with ED and multiple risk factors had poorer QoL than men with ED and no risk factors (49).

Lastly, summarizing the somewhat contradictory findings of studies done by authors during current pandemic: the opportunity for physical intimacy that prolonged confinement and forced coexistence resulting from lockdown has created is undeniable. An online survey from the United Kingdom showed that, during the period of self-isolation, about two-fifth of the respondents reported to have had sex at least once in a week (50). But for others, stress and extended proximity to one's partner exacerbate differences in desire, as cited by a recent study conducted in India exploring the same circumstance (51). Yet, it led to an improvement in overall relationship with the partners, communication with the partner, and reduction in the interpersonal conflicts.

Strengths and Limitations

This is not the first study to investigate sexual activity during the COVID-19 self-isolation/social distancing, but research data in the subcontinent in this topic are not vast. The findings, despite the novelty, must be interpreted in light of the limitations. Since this was an online survey, youths in their 30s constituted majority of the participants considering their familiarity with social media.

In addition, only a population fluent in English participated. Taboo and stigma attached to sexuality might have been the reason that limited female volunteers more in the survey, given that 80% of the participants were male. This lack of female participation has been observed by prior researchers working on sexual side effects of antipsychotics (52). There is scope of measurement bias, as participants were asked to self-report their sexual activity, mental health status, and quality of life, all of which may be subjected variable mental computing mechanisms at the time of reporting, resulting in a systematic deviation. While use of GSEM makes the analysis robust, introduction of different levels of variables may have affected the model estimation, which was outside the scope of this study to analyze further. The analyses were cross-sectional, and thus, it is not possible to determine trajectories of sexual activity during the current pandemic. Pre-COVID data were not collected for comparison, and significant areas of sexual behavior queries like masturbatory habit, consumption of pornographic material, or homosexual relationship were not included in the questionnaire.

Implications/Recommendations

Findings from the present study shed light on sexual activity during COVID-19 self-isolation/social distancing among Indian subpopulation. These findings suggest that interventions to promote good mental and physical health during the COVID-19 self-isolation/social distancing period should take into account positive sexual health. The psychological burden self-isolation/social distancing must not be translated into the vicious cycle of poor state of sexual health to poorer state of mental health. A view of sex and intimacy as a mode of positive coping and social connection building might be promoted under a non-prejudiced mindset. Addressing the unmet need of women suffering from sexual disorder is the need of the hour. One must

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be vigilant to the burden of non-communicable disease and of mental morbidity in youth that emerged as a collateral finding.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Institutional Ethics Committee, Diamond Harbour Government Medical College and Hospital. The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

SC and RB: conceptualization, methodology, investigation, writing—original draft, and project administration. AC: methodology, validation, and writing—review and editing. AL: conceptualization, methodology, formal analysis, writing—review and editing, and supervision. AD: software, formal analysis, and writing—review and editing. All authors contributed to the article and approved the submitted version.

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A Prospectively Validated Nomogram for Predicting the Risk of PHQ-9 Score ≥15 in Patients With Erectile Dysfunction: A Multi-Center Study

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*Correspondence:

Jianlin Yuan jianliny@fmmu.edu.cn Emmanuele A. Jannini eajannini@gmail.com

[†]These authors have contributed equally to this work and share first authorship

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Yu Zheng ^{1,2,3†}, Ming Gao ^{4†}, Guangdong Hou ^{1†}, Niuniu Hou ^{5†}, Xiao Feng ², Tommaso B. Jannini ⁶, Di Wei ¹, Wanxiang Zheng ¹, Lei Zhang ¹, Xinlong Dun ¹, Geng Zhang ¹, Fuli Wang ¹, Ping Meng ¹, Emmanuele A. Jannini ^{6*} and Jianlin Yuan ^{1*}

¹ Department of Urology, Xijing Hospital, Air Force Medical University, Xi'an, China, ² Department of Anatomy, Histology and Embryology, Air Force Medical University, Xi'an, China, ³ Medical Innovation Center, Air Force Medical University, Xi'an, China, ⁴ Department of Andrology, Xi'an Daxing Hospital, Shaanxi University of Chinese Medicine, Xi'an, China, ⁵ Department of General Surgery, Eastern Theater Air Force Hospital of PLA, Nanjing, China, ⁶ Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy

Background: Although erectile dysfunction (ED) often occurs simultaneously with depression, not all patients with ED suffer major depression (MD), with a PHQ-9 score ≥15 indicating MD. Because the PHQ-9 questionnaire includes phrases such as "I think I am a loser" and "I want to commit suicide," the psychological burdens of ED patients are likely to increase inevitably after using the PHQ-9, which, in turn, may affect ED therapeutic effects. Accordingly, we endeavored to develop a nomogram to predict individual risk of PHQ-9 score ≥15 in these patients.

Methods: The data of 1,142 patients with ED diagnosed in Xijing Hospital and Northwest Women and Children's Hospital from January 2017 to May 2020 were analyzed. While the Least Absolute Shrinkage and Selection Operator regression was employed to screen PHQ-9 score ≥15 related risk factors, multivariate logistic regression analysis was performed to verify these factors and construct the nomogram. The training cohort and an independent cohort that comprised 877 prospectively enrolled patients were used to demonstrate the efficacy of the nomogram.

Results: The IIEF-5 score, PEDT score, physical pain score, frequent urination, and feeling of endless urination were found to be independent factors of PHQ-9 score ≥15 in patients with ED. The nomogram developed by these five factors showed good calibration and discrimination in internal and external validation, with a predictive accuracy of 0.757 and 0.722, respectively. The sensitivity and specificity of the nomogram in the training cohort were 0.86 and 0.52, respectively. Besides, the sensitivity and specificity of the nomogram in the validation cohort were 0.73 and 0.62,

respectively. Moreover, based on the nomogram, the sample was divided into low-risk and high-risk groups.

Conclusion: This study established a nomogram to predict individual risk of PHQ-9 score ≥15 in patients with ED. It is deemed that the nomogram may be employed initially to avoid those with a low risk of MD completing questionnaires unnecessarily.

Keywords: erectile dysfunction, major depression, nomogram, prognostic factor, risk factor

INTRODUCTION

Erectile dysfunction (ED), which is one of the most common andrological diseases, refers to the inability of men to obtain and maintain sufficient erections continuously to complete satisfactory sexual intercourse. ED mostly affects men over the age of 40 years and has a considerable incidence throughout the world. The EAU 2021 Andrology Disease Guide notes that the incidence of ED, which ranges from 12 to 82.9%, increases with age (1). An epidemiological survey in China revealed that the comprehensive prevalence of ED is as high as 49.69%. Furthermore, 20.86, 25.3, 40.48, 60.12, 79.1, and 93.72% of men aged under 30 years, between 30 and 39, 40 and 49, 50 and 59, 60 and 69, and over 70 years, respectively suffer ED (2). Although ED is not life-threatening, it may leave those affected feeling inferior, embarrassed, anxious, and depressed, which may have an adverse effect on their quality of life.

It is well established in the literature that major depression (MD) is consistently associated with sexual dysfunction (SD). Indeed, SD may be the result of either the pathophysiology of the disease itself or the psychopharmacotherapy patients with MD frequently undergo (3). Among sexual impairments, absent or delayed orgasm, premature ejaculation (PE), decreased libido, difficulties with arousal, and ED are listed as the most common ones (4). Although ED is one of the most common male diseases, which often occurs in conjunction with depression, the "chickenand-egg relationship" between ED and depression remains unclear (5). Some studies have shown that both conditions share a common pathophysiological basis, with the one affecting the other (6-9). Shiri et al. (10) found that the incidence of ED was 59/1,000 person-years (95% confidence interval [CI] 39-90) in men with depressive mood and 37/1,000 person-years (95% CI 32-43) in those free of the disorder. Moreover, a recent systematic review and meta-analysis reported pooled odds ratio (OR) for risk of ED among patients with MD was 1.39 (11). For these reasons, it is imperative that patients with MD should be routinely screened for ED, and, on the contrary, patients with ED must be routinely screened for MD (12). To this end, the psychological evaluation of patients with ED is of paramount importance for two reasons. Firstly, patients with ED usually experience PE, which, in turn, is a risk factor for depression (13); secondly, the first-line PE treatment selective serotonin reuptake inhibitors (SSRIs) may frequently concur to produce ED while treating ejaculation impairments (14).

There are many scales used to screen for depression, such as the 9-item version of the Patient Health Questionnaires

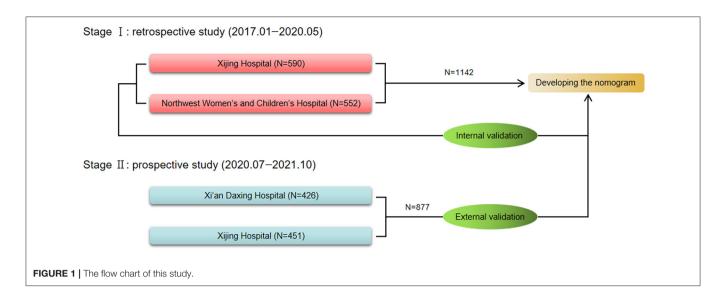
(PHQ-9), Beck Depression Inventory-II (BDI), Center for Epidemiological Studies-Depression Scale-20 (CES-D), Common Mental Disorder Questionnaireare (CMDQ) and so on (15). Among these methods, PHO-9 has been reported to be an easy-to-use and the most reliable one, with a total score of \geq 15 considered as an MD candidate (16). However, routine clinical practice shows that the psychological burdens of ED patients may increase more or less after using the PHQ-9 because it includes phrases such as "I think I am a loser" and "I want to commit suicide". In turn, these PHQ-9-induced psychological burdens may have a negative impact on ED therapy. Therefore, we endeavored to develop a nomogram to predict individual risk of PHQ-9 score >15 in patients with ED, so that the treatment outcomes of patients with low risk of PHQ-9 score ≥15, who should be provided with close follow-up rather than the PHQ-9, may be improved.

MATERIALS AND METHODS

Study Sample

The training cohort comprised 1,142 patients with ED diagnosed at Xijing Hospital (Xi'an, China) and Northwest Women and Children's Hospital (Xi'an, China) from January 2017 to May 2020. The data of the patients in this cohort were retrospectively analyzed to explore independent predictors of MD and develop the nomogram. After the completion and internal validation of the nomogram, the data of patients with ED diagnosed in Daxing hospital (Xi'an, China) and Xijing Hospital (Xi'an, China) from July 2020 to November 2021 were collected prospectively. Finally, the data of 877 patients were collected and employed as an independent verification cohort for external verification of the nomogram. The flowchart of this study is depicted in **Figure 1**.

The inclusion and exclusion criteria of all the patients in the cohort that established and verified the model are as follows. The patients had to be at least 18 years old, involved in a monogamous sexual relationship and have had vaginal intercourse for at least 2 months, have had sexual intercourse at least once a month during the previous 2 months, not taken drugs such as antidepressants and type 5 phosphodiesterase inhibitors that may have affected their ability to have an erection during the previous 2 months, not suffer from any other serious neurological and/or mental disorders, and ensure that all information provided was correct. Two experienced urologists employed the diagnostic criteria of the International Society of Sexual Medicine (ISSM) (17) to diagnose ED. The



PHQ-9 was employed to assess MD and as noted previously, a total score of \geq 15 was considered MD candidate (13). All the patients who participated in the study provided written informed consent. Furthermore, all the procedures performed in our study were approved by the ethics committee of Xijing Hospital (No. KY20212177-F-1).

Variable Selection

The variables included in this study were age at visit, residence (town/city or countryside), income, years of education, the 5-item International Index of Erectile Function (IIEF-5) questionnaire score (18), premature ejaculation diagnostic tool (PEDT) score (19), frequency of sexual desire, feeling of endless urination, and frequent urination, that is, having to urinate within 2h of urinating during the previous 2 weeks. In addition, their average physical body pain intensity during the previous 2 weeks was evaluated by employing the short form of the Brief Pain Inventory (20), which assesses pain on a numerical scale, ranging from 0 (no pain) to 10 (the most severe pain imaginable). According to the IIEF-5 score, erectile function is divided into four grades: without ED (≥22), mild ED (12-21), moderate ED (8-11), and severe ED (5-7).

Statistical Analysis

The Kolmogorov Smirnov test demonstrated the discrete variables and only continuous variable, namely, age at visit to be a nonnormal distribution as frequency (proportion) and median (interquartile range), respectively. While the distribution of discrete variables between the training and validation cohorts was evaluated by means of a chi square test, the Mann–Whitney *U*-test was employed to assess the distribution of age at visit. The Least Absolute Shrinkage and Selection Operator (LASSO) (21) was adopted to reduce the dimensionality of the data and prevent the model from overfitting (22). The nomogram was developed using R software (version 4.0.3) by integrating

independent predictors identified by multivariable logistic regression models. In the internal verification, the calibration chart of the nomogram was drawn by comparing prediction and observation. The discrimination of the nomogram was reflected by the area under the curve (AUC) of the receiver operating characteristic (ROC) (23), ranging from 0.5 (equivalent to tossing a coin) to 1 (implying excellent discrimination). Furthermore, 1,000-times-repeated bootstrapping resampling was performed for these evaluations. The sensitivity and specificity of the nomogram were identified according to the maximum Youden index on the basis of the ROC curve. Similarly, in the external verification, a calibration chart was drawn, and AUC was calculated to verify the performance of the nomogram further. Moreover, restricted cubic splines analyses based on logistic regression models with five knots (at the 5th, 27.5th, 50th, 72.5th, and 95th percentiles) of the continuous total points were performed to assess the exposure-response relationship between the predictive point and MD (24).

Two-tailed P values < 0.05 were considered to be statistically significant.

RESULTS

Characteristics of Patients and Variables

The proportion of PHQ-9 score \geq 15 in the training cohort and validation cohort are 12.4% (142/1,142) and 11.6% (102/877), respectively. The characteristics of the two cohorts are displayed in **Table 1**. No statistical difference between the two cohorts was found in the comparison of the 10 basic variables (all P > 0.05; **Table 1**). Besides, the PHQ-9 scores in the two cohorts are 7 (4–11) and 7 (4–11), respectively (P = 0.859). In the training cohort, patients from the western, central, and eastern regions of China accounted for 57.8% (660/1,142), 26.5% (303/1,142), and 15.7% (179/1,142), respectively, and the proportions in the validation cohort were 51.4% (451/877), 27.7% (243/877), and 20.9% (183/877), respectively.

TABLE 1 | Comparison of variables between training cohort and validation cohort.

Variables	Training cohort	Validation cohort	P-Value
	(N=1,142)	(N = 877)	
Age at visit (years), n (%)			
≤25	196 (17.2)	137 (15.6)	0.617
26–30	413 (36.2)	320 (36.5)	
31–35	307 (26.9)	229 (26.1)	
>35	226 (19.8)	191 (21.8)	
Residence, n (%)			
town/city	864 (75.7)	682 (77.8)	0.268
countryside	278 (24.3)	195 (22.2)	
Income (RMB/month), n (%)			
<5,000	787 (68.9)	573 (65.3)	0.236
5,000-10,000	273 (23.9)	234 (26.7)	
>10,000	82 (7.2)	70 (8.0)	
Years of education, n (%)			
Years ≤ 9	229 (20.1)	168 (19.2)	0.637
9 < years <16	532 (46.6)	399 (45.5)	
Years ≥16	381 (33.4)	310 (35.3)	
IIEF-5 score, n (%)			
5–7	73 (6.4)	59 (6.7)	0.965
8–11	204 (17.9)	155 (17.7)	
12–16	406 (35.6)	304 (34.7)	
17–21	459 (40.2)	359 (40.9)	
PEDT score, n (%)			
≤8	181 (15.8)	162 (18.5)	0.400
9–10	104 (9.1)	77 (8.8)	
11–14	348 (30.5)	271 (30.9)	
≥15	509 (44.6)	367 (41.8)	
Physical pain score, n (%)			
0	613 (53.7)	494 (56.3)	0.611
1	316 (27.7)	220 (25.1)	
2	81 (7.1)	67 (7.6)	
3	65 (5.7)	43 (4.9)	
≥4	67 (5.9)	53 (6.0)	
Frequency of sexual desire, n (%)	. ,	, ,	
Hardly any	281 (24.6)	201 (22.9)	0.550
A few times	358 (31.3)	282 (32.2)	
About half the time	441 (38.6)	335 (38.2)	
Most of the time	62 (5.4)	59 (6.7)	
Frequent urination, n (%)	,	. ,	
Hardly any	720 (63.0)	546 (62.3)	0.730
A few times	158 (13.8)	136 (15.5)	
About half the time	129 (11.3)	92 (10.5)	
Most of the time	135 (11.8)	103 (11.7)	
Feeling of endless urination, <i>n</i> (%)		(
Hardly any	773 (67.7)	593 (67.6)	0.732
A few times	138 (12.1)	103 (11.7)	5 02
About half the time	74 (6.5)	49 (5.6)	
Most of the time	157 (13.7)	132 (15.1)	

IIEF-5, 5-item International Index Erectile Function; PEDT, premature ejaculation diagnostic tool.

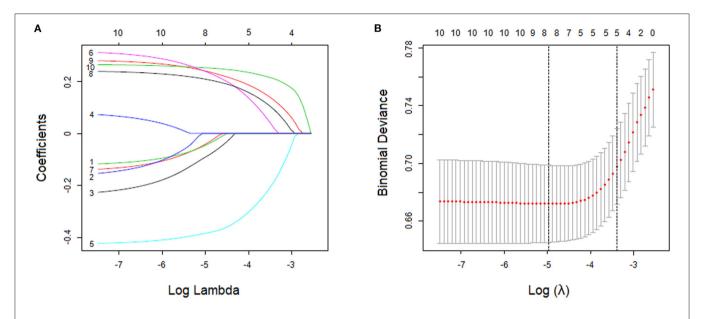


FIGURE 2 | Variable screening using the least absolute shrinkage and selection operator (LASSO) binary logistic regression model. **(A)** LASSO coefficient profile of features. This graph shows the relationship between the penalty coefficient $\log(\lambda)$ and the retained charicteristics. The number of intersecting curves represent the number of charicteristics retained at that $\log(\lambda)$ value. **(B)** The relationship between $\log(\lambda)$ and binomial deviance. Based on the 10-fold crossvalidation method, the relationship between $\log(\lambda)$ and binomial deviance is drawn. The dotted vertical lines were drawn at the optimal values by using the minimum criteria and the minimum criterion of 1 SE.

The Selection of Predictors and the Construction of the Nomogram

With nonzero coefficients in the LASSO regression, five potential predictors (IIEF-5 score, PEDT score, physical pain score, frequent urination, and feeling of endless urination) were selected from the 10 variables included in the study (**Figures 2A,B**). The AUCs of the IIEF-5 score, PEDT score, physical pain score, frequent urination, and feeling of endless urination in the training cohort were 0.639, 0.605, 0.631, 0.658, and 0.667, respectively. Furthermore, the AUCs of these variables in the validation cohort were 0.625, 0.610, 0.626, 0.613, and 0.632, respectively.

All the five potential predictors selected by the LASSO regression were independent predictors when the multivariate logistic regression analysis was performed. All odd ratio and *P* values are presented in **Table 2**. R software was employed to integrate these five independent predictors and develop the nomogram in accordance with the regression coefficients of these predictor variables (**Figure 3**).

Evaluation of the Nomogram

In the training cohort, the AUC of the nomogram was 0.757 (95% CI: 0.754–0.760), which proves the mid-to-high discrimination ability thereof. In addition, the AUC of the nomogram was statistically higher than the IIEF-5 (0.757 vs. 0.639, P < 0.001), PEDT (0.757 vs. 0.605, P < 0.001), physical pain score (0.757 vs. 0.631, P < 0.001), frequent urination (0.757 vs. 0.658, P < 0.001), and feeling of endless urination

(0.757 vs. 0.667, P < 0.001; **Figure 4A**). Similarly, in the validation cohort, the nomogram AUC was 0.722 (95% CI: 0.718–0.726), which also demonstrates an AUC higher than other factors such as the IIEF-5 (0.722 vs. 0.625, P < 0.001), PEDT (0.722 vs. 0.610, P < 0.001), physical pain score (0.722 vs. 0.626, P < 0.001), frequent urination (0.722 vs. 0.613, P < 0.001), and feeling of endless urination (0.722 vs. 0.632, P < 0.001; **Figure 4B**). Additionally, the sensitivity and specificity of the nomogram in the training cohort are 0.86 and 0.52, respectively; and the sensitivity and specificity in the validation cohort are 0.73 and 0.62, respectively. In the training cohort, good consistency between the predicted possibility and actual rate was observed (**Figure 4C**). Furthermore, in the validation cohort, excellent calibration of the nomogram was realized (**Figure 4D**).

Dose-Response Analysis

Dose-response analysis demonstrated a nonlinear relationship between the nomogram-predicted total points and PHQ-9 score \geq 15 (overall association P < 0.001, nonlinear P = 0.030). The risk of PHQ-9 score \geq 15 was relatively flat until approximately 180 points of the total-points level and then started to increase rapidly (P for nonlinearity < 0.05). Therefore, 180 points was identified as a reference according to the trend of the restricted cubic spline and accordingly, the participants were divided into low-risk and high-risk groups. The PHQ-9 score \geq 15 rates of the two groups were 7.57 and 16.09%, respectively. The overall risk of MD in the high-risk group was 2.34 (95% CI 1.75–3.13) times higher than that of low-risk group (**Figure 5**).

TABLE 2 | Multivariable logistic regression of predictors for screening major depression in patients with erectile dysfunction (training cohort).

Variables	OR	95% CI	P value
IIEF-5 score			<0.001
17–21	1 (reference)		
12–16	1.582	0.974-2.569	0.064
8–11	2.637	1.558-4.463	<0.001
5–7	3.669	1.864–7.221	< 0.001
PEDT score			0.023
≤8	1 (reference)		
9–10	2.065	0.783-5.449	0.143
11–14	2.377	1.094–5.165	0.029
≥15	3.070	1.469-6.414	0.003
Physical pain score			0.041
0	1 (reference)		
1	1.409	0.886-2.238	0.147
2	1.580	0.803–3.108	0.185
3	2.049	1.037-4.049	0.039
≥4	2.552	1.319-4.936	0.005
Frequent urination			0.038
Hardly any	1 (reference)		
A few times	1.538	0.891–2.656	0.122
About half the time	1.686	0.934–3.044	0.083
Most of the time	2.277	1.275-4.068	0.005
Feeling of endless urination			0.026
Hardly any	1 (reference)		
A few times	1.636	0.927–2.888	0.090
About half the time	1.951	0.986–3.862	0.055
Most of the time	2.223	1.275–3.876	0.005

CI, confidence interval; IIEF-5, 5-item International Index Erectile Function; OR, odd ratio;

PEDT, premature ejaculation diagnostic tool.

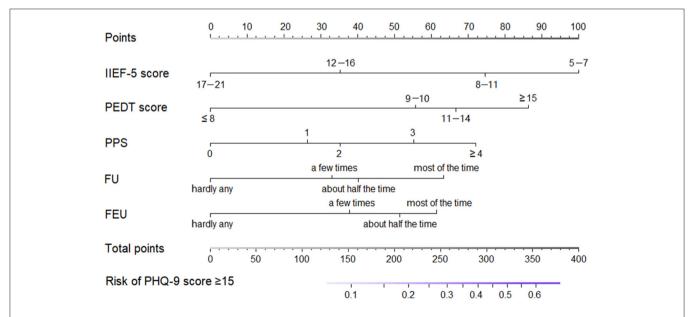


FIGURE 3 | Nomogram for predicting individual risk of major depression in patients with erectile dysfunction. (IIEF-5, 5-item International Index Erectile Function; PEDT, premature ejaculation diagnostic tool; PPS, physical pain score; FU, frequent urination; FEU, feeling of endless urination).

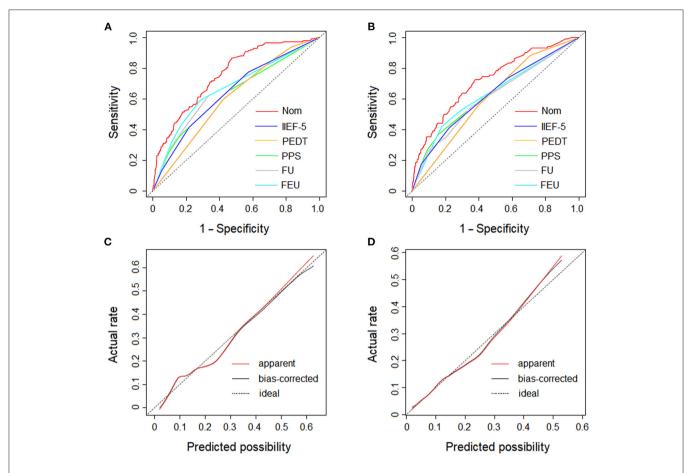


FIGURE 4 | The ROC curves and the dotted line represents of the derivation cohort and validation cohort. (A) The ROC curves of the nomogram, IIEF-5 score, PEDT score, physical pain score, frequent urination and feeling of endless urination in derivation cohort. (B) The ROC curves of the nomogram, IIEF-5 score, PEDT score, physical pain score, frequent urination and feeling of endless urination in validation cohort. (C) The calibration plot of the nomogram in derivation cohort. (D) The calibration plot of the nomogram in validation cohort. The dotted line represents the calibration of an ideal nomogram (the predicted risk perfectly corresponds to the actual rate). The red solid line represents the apparent accuracy of the nomogram without correction for overfitting, while the black solid line represents the bootstrap-corrected nomogram. (Nom, nomogram; IIEF-5, 5-item International Index Erectile Function; PEDT, premature ejaculation diagnostic tool; PPS, physical pain score; FU, frequent urination; FEU, feeling of endless urination).

DISCUSSION

The PHQ-9 is the most reliable tool for screening depression. But it may carry the risk of having adverse side effects on patients with ED who tend to worry that their condition will advance as described in the scale. Therefore, it is necessary to develop a nomogram to predict individual risk of PHQ-9 score \geq 15 before using the PHQ-9, which may help clinical decision making.

The nomogram confirmed that the IIEF-5 score and PEDT score were independent risk factors for MD. First, the IIEF-5 score and PEDT score reflect the state of male sexual life jointly and depression has been found to be related to a decrease of sexual activity in male patients (25). Second, as observed in clinical practice, PE often occurs simultaneously with ED, thus resulting in a vicious circle, recently described as Loss of Control over Erection and Ejaculation (LCEE) (26). When a man with ED tries to achieve or maintain an erection through strong stimulation, his precoital excitement may be higher than that

of normal healthy men, which results in shorter intravaginal ejaculation latency time. Similarly, when a patient with PE attempts to control ejaculation, his level of sex excitement decreases instinctively, which may lead to ED (27, 28). Finally, SSRIs used in the treatment of PE and MD may cause ED (3). Depending on the various drugs, the incidence of ED may range from 25.8 to 80.3% (14). Unfortunately, ED may persist after SSRIs are discontinued, with this treacherous condition being only recently defined as post-SSRI sexual dysfunction (PSSD) (29, 30).

Physical pain is another independent risk factor for MD. Research has revealed that between 30 and 60% of patients who suffer chronic pain have a depressive state (31), and more than 60% of patients with MD experience physical pain (32). This suggests that somatic pain and MD are closely related. Its mechanisms may include a high overlap of brain regions involved in depression and pain (33) because they share a common underlying brain network (34); Furthermore, inflammatory

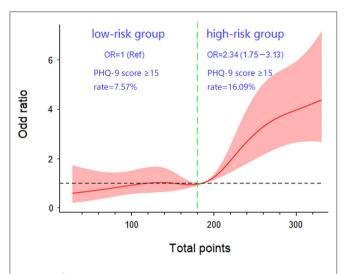


FIGURE 5 | Dose-response association between total points. The presence of major depression in patients with erectile dysfunction with five knots located at the 5th, 27.5th, 50th, 72.5th, and 95th percentiles. (Ref, reference; OR, odds ratio).

inducible factors such as Interleukin-1B may induce depression-like behavior and cause hyperalgesia. Finally, the HPA axis may be involved in the interaction between depression and pain (35).

Frequent urination and feeling of endless urination may be classified in the category of lower urinary tract symptoms (LUTS). Research throughout the world has shown that LUTS are related to ED and depression (36-38). Frequent urination and feeling of endless urination are also independent risk factors for MD in our nomogram. The common pathophysiological mechanisms of LUTS and ED include changes in the nitric oxide/cGMP pathway in the prostate and penis, rho kinase activation, endothelial pathway regulation, autonomic overactive pathways, and changes secondary to pelvic atherosclerosis (39). The correlation between LUTS and depression is longestablished, with the first one being associated with a poor quality of life and therefore leading to depressive symptoms (40). Furthermore, also a reduction of serotonin in the brain has been documented. This neurochemical change in the central nervous system that may is well-known to be associated with depression may also affect the autonomic nervous activity that regulates the urinary tract, thus resulting in LTUS (41).

This work suffers from a number limitations. Firstly, although it is a multicenter study, data were collected from only three centers. Despite the three sampling centers being located in Xi'an, Shaanxi Province, China, only 29.7% (339/1,142) and 30.1% (267/877) of the two cohorts were from Shaanxi Province. However, the sample includes most areas in China and therefore, has a certain degree of representativeness. Secondly, the IIEF-5 and PEDT scales in the study are self-assessment scales, which may have led to an overestimation of the results because of the subjective nature thereof.

CONCLUSIONS

In this study, a nomogram that can predict the risk of patients with ED of being comorbid with PHQ-9 score $\geq\!15$ was developed, and the stability of the nomogram was verified through an independent cohort. According to the nomogram, patients with ED can be divided into a low-risk group and highrisk group. While the first had an PHQ-9 score $\geq\!15$ rate of 7.57%, that of the second one was 16.09%. Hence, it is recommended that patients in the high-risk group complete the PHQ-9 and those in the low-risk group are monitored closely. This may avoid the potential adverse effects patients with a low risk may suffer when completing the PHQ-9. It is recommended that the nomogram should be evaluated on a large sample.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

All the procedures performed in our study were approved by the ethics committee of Xijing Hospital (No. KY20212177-F-1). The patients/participants provided their written informed consent to participate in this study.

AUTHOR CONTRIBUTIONS

Concept and design: JY, EJ, YZ, and GH. Acquisition, analysis, or interpretation of data: MG, GH, XF, YZ, LZ, and XD. Drafting of the manuscript: YZ, GH, MG, and NH. Critical revision of the manuscript: EJ, JY, NH, and TJ. Statistical analysis: DW, WZ, and GH. Obtained funding: JY, EJ, and MG. Administrative, technical, or material support: GZ, PM, and FW. Supervision: JY and EJ. All authors contributed to the article and approved the submitted version.

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EDITED BY
Patrik Roser,
University of
Duisburg-Essen, Germany

REVIEWED BY
Markus Zedler,
Hannover Medical School, Germany
Carlos Miguel Rios-González,
National University of
Caaquazú, Paraquay

*CORRESPONDENCE Juan Carlos Sierra jcsierra@ugr.es

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Masturbation parameters related to orgasm satisfaction in sexual relationships: Differences between men and women

Oscar Cervilla and Juan Carlos Sierra*

Mind, Brain, and Behavior Research Center (CIMCYC), University of Granada, Granada, Spain

Objective: Masturbation is a behavior that can enhance sexual functioning. This study aims to analyze differences between men and women in different masturbation parameters, and to examine their relation with orgasm satisfaction in sexual relationships.

Method: One thousand three hundred and thirty-fifth men and women from the Spanish population aged 18-83 years (M=36.91; SD=11.86) participated in an online survey. A questionnaire was used to collect socio-demographic. Sexual history data, negative attitude toward masturbation, solitary sexual desire and orgasm subjective experience upon masturbation were assessed. Given the differences between men and women, independent regression models are proposed to explain orgasm satisfaction in the sexual relationships context.

Findings: Men, compared to women, masturbated at a younger age (p < 0.001), and reported higher current masturbation frequency (p < 0.001) and more solitary sexual desire (p < 0.001). Women reported greater intensity in the subjective orgasm experience on its Affective (p < 0.001), Sensory (p < 0.001) and Intimacy (p < 0.001) dimensions. Regarding regression models, the Affective dimension of orgasm was a common parameter in men (p = 0.36), p < 0.001) and women (p = 0.24) to explain orgasm satisfaction during sexual relationships. In men, solitary masturbation frequency (p = 0.01), p = 0.027) acquired a significant role. In women, the model also included age (p = 0.001) and solitary sexual desire (p = 0.019), p = 0.001).

Conclusion: When dealing with men and women's orgasm difficulties in the sexual relationships context, it is important to consider the role of masturbation. In men and women, the Affective dimension of the orgasm experience explain the orgasm satisfaction in sexual relationship. Also, in men, the solitary masturbation frequency is negatively related with orgasm satisfaction in sexual relationship, supporting the compensatory hypothesis of masturbation. In women, in addition to the Affective dimension, the orgasm satisfaction in sexual relationship is explained, negatively, by the negative

attitude toward masturbation, and positively, by the solitary sexual desire, which could be associated with more sexual self-knowledge. The relevance of masturbation in understanding sexual functioning is highlighted.

VEVMODDS

orgasm satisfaction, partnered sex, masturbation, subjective orgasm experience, attitude toward masturbation, sex differences

Introduction

Masturbation is a relatively frequent behavior that is positively associated with sexual health (1-5). More importance has been attached to study it in recent decades, and its capacity to promote sexual self-knowledge and to elicit positive sexual responses has been underlined (6,7). Among these good points, its usefulness in sexual therapy to improve sexual functioning has been stressed (8).

Very little evidence exists for the relation between masturbation and sexual relationships (9). The association between both sexual behaviors has been described by two models: compensatory vs. complementary. The former proposes practicing masturbation to replace desired sexual relationships that do not take place (10, 11). The fact that higher masturbation frequency is related to lower sexual satisfaction, and has been found for women, favors this model (12), while higher masturbation frequency for those who less enjoy their sexual relationships has been described for men (13). The complementary model hypothesizes that a direct positive relation exists between both these sexual activities, and increasing the practice of one would be associated with an increase in the other (14).

Some works suggest that masturbation does not offer a clear advantage for sexual relationships (15–17). Nonetheless, it has been found that women who masturbate are more likely to have an orgasm during sexual relationships (18), and those who masturbate more frequently describe better sexual experiences in couples and less sexual inhibition (2, 3). Techniques like Directed Masturbation can boost pleasurable stimulation from knowing pleasure points, which improves women's orgasm facility while couples practice sex (19). Therefore, learning to have orgasms by masturbation allows women to adjust and generalize this orgasm response in sexual relationships in couples (20). These results sustain the usefulness of masturbation as the first line of treatment for the Female Orgasmic Disorder (20, 21).

Despite some findings that favor practicing masturbation to improve orgasm capacity, very little evidence exists for the role that the different parameters related to this behavior play in orgasms in the sexual relationships context. Of these parameters, attitude toward masturbation, solitary sexual desire

and intensity of the subjective orgasm experience obtained by masturbation stand out. Taking a negative attitude toward masturbation has been associated with feeling guilty and ashamed (22, 23), and also with negative sexual experiences (24). Moreover, lower masturbation frequency, more difficulty to have an orgasm and lower orgasm satisfaction have been observed in those with a more negative attitude toward masturbation (25). Solitary sexual desire (i.e., interest in solitary sexual activity) has been associated with high sexual satisfaction and self-esteem levels in women (2, 4), and has been related to both sexual satisfaction and unsatisfactory sexual functioning in men (26-28). In light of all this, a positive relation between solitary sexual desire and the intensity of the subjective orgasm experience in the solitary masturbation context has been found in a sample made up of men and women (29). Subjective orgasm experience in masturbation has been shown to be capable of distinguishing people with and without difficulties in having an orgasm during sexual relationships (29). Sierra et al. (30) recently observed that masturbation frequency, negative attitude toward masturbation and the subjective orgasmic experience in masturbation are associated with orgasm satisfaction in sexual relationships in people aged over 50 years.

Bearing in mind the relevance of masturbation for sexual health, and its usefulness in the therapeutic context to improve sexual functioning, this study aims to: analyze differences between men and women in different masturbation parameters (i.e., first masturbation experience, current solitary masturbation frequency, negative attitude toward masturbation, solitary sexual desire and subjective orgasm experience); examine their relation, along with age, to orgasm satisfaction in the sexual relationships context. To do so, the following hypotheses are proposed: (1) differences are expected in masturbation parameters between men and women; (2) orgasm satisfaction in sexual relationships is expected to be linked with masturbation parameters (30).

Methods

Participants

The sample comprised 1,335 Spanish adults (738 men, 597 women) aged 18–83 years ($M=36.91;\ SD=11.86$). The

TABLE 1 Sociodemographic characteristics of the participants.

Variables	Total $N = 1,335$	Men n = 738	Women $n = 597$
Age M (SD)	36.91 (11.86)	37.62 (12.43)	36.04 (11.07)
Level of education n (%)			
Primary education	53 (4.0)	26 (3.5)	27 (4.5)
Secondary education	390 (29.2)	231 (31.3)	159 (26.6)
University degree (ongoing or completed)	892 (66.8)	481 (65.2)	411 (68.9)
Currently have a partner n (%)			
Yes	988 (74.0)	524 (71.0)	464 (77.7)
No	347 (26.0)	214 (29.0)	133 (22.3)
Praying frequency n (%)			
Never	989 (74.1)	523 (70.90)	466 (78.1)
Less than once a month	123 (9.2)	67 (9.1)	56 (9.4)
Once a month	7 (0.5)	6 (0.8)	1 (0.2)
A few times a month	54 (4.0)	32 (4.3)	22 (3.7)
Once a week	8 (0.6)	3 (0.4)	5 (0.8)
A few times a week	57 (4.3)	34 (4.6)	23 (3.9)
Once a day	60 (4.5)	41 (5.6)	19 (3.2)
More than once a day	37 (2.8)	32 (4.3)	5 (0.8)

inclusion criteria were: (a) having Spanish nationality; (b) being heterosexual; (c) currently engaging in sexual relationships; (d) having solitary masturbation experience. Table 1 shows the samples' socio-demographic characteristics.

Measures

Background questionnaire. This instrument collects data about sex, age, level of education, nationality, sexual orientation, partner relationship, frequency of prayer, age when the first masturbation experience occurred and masturbation frequency.

The Spanish version of the Negative Attitudes Toward Masturbation Inventory (NATMI) (25, 31). It evaluates negative attitudes toward masturbation with 10 items (e.g., "I feel guilty about masturbating") answered on a 5-point Likert-type scale: 1 (Not at all true for me) to 5 (Extremely true for me). Higher scores indicate a more negative attitude toward masturbation. It has a high internal consistency (alpha ordinal) of 0.95, and presents suitable evidence for construct and discriminant validity with other psychosexual variables and sexual functioning. In this sample, the ordinal alpha coefficient was 0.91.

The Solitary Sexual Desire subscale from the Spanish version of the Sexual Desire Inventory (SDI) (28, 32). It consists of four items (e.g., "How strong is your desire to engage in sexual behavior by yourself?") and measures interest in solitary sexual

activity using different Likert response scales depending on the item (e.g., from 0 = No desire to 8 = Strong desire). Higher scores show more solitary desire. It presents good internal consistency (Cronbach's α higher than 0.90) and evidence for external validity. Cronbach's alpha in the present study was 0.91.

The Spanish version of the Orgasm Rating Scale (ORS) (33) adapted to the solitary masturbation context by Cervilla et al. (29). It assesses the subjective orgasm experience in the solitary masturbation context (during any sexual activity performed alone) with 25 adjectives distributed on four dimensions: Affective, Sensory, Intimacy, and Rewards. Items are answered on a 6-point Likert-type scale: 0 (Does not describe it at all) to 5 (Describes it perfectly). Higher scores indicate more intensity in the subjective orgasm experience. Its internal consistency reliability is good and ranges from 0.71 to 0.95. It adequately evidences validity, provided by its measures. In our study, the ordinal alphas for the different subscales were: 0.93 for Affective, 0.94 for Sensory, 0.72 for Intimacy and 0.89 for Rewards.

The Spanish version of the Arizona Sexual Experience Scale (ASEX) (34) of Sánchez-Fuentes et al. (35). It consists of five items that assess general sexual functioning (sexual desire, arousal, erection for men/lubrication for women, orgasm, and orgasm satisfaction) in the last 7 days in the sexual relationship context. It uses a Likert-type scale from 1 (hypofunction) to 6 (hyperfunction). It presents good internal consistency (Cronbach's alpha of 0.81 in men, 0.79 in women) and evidences validity. The orgasm-related item referring to orgasm satisfaction was taken into account. Its score was inverted, so higher scores evidenced more orgasm satisfaction.

Procedure

Data collection was conducted by distributing a survey using LimeSurvey, which was promoted by paying to Facebook (900€) from 23 December 2019 to 15 March 2020 by adults from Spain. In order to improve the representativeness of the sample, the promotion targeted both men and women from different age groups. Online assessments are normally used to evaluate sexual behaviors (1, 36, 37). Previous studies have confirmed that there are no differences between online and paper-and-pen methods (38, 39). To avoid automatic or fraudulent responses, IP was controlled and a CAPTCHA was used. In addition, responses were carefully examined to rule out non conclusive or abnormal cases. Participation was voluntary, and both anonymity and confidentiality of responses were guaranteed. There was no compensation for taking part in the study. All the participants received informed consent with the study aim before responding. This research was approved by the Ethics Committee of Human Research of the University of Granada.

TABLE 2 Effects of sex on masturbation-related indicators.

Variables M (DT)	Males $n = 738$	Females $n = 597$	$F_{(1, 1, 329)}$	p	Cohen's d
First masturbation experience	12.60 (2.03)	15.13 (5.92)	140.51	< 0.001	0.60
Current frequency of solitary	3.17 (0.94)	2.50 (0.96)	185.11	< 0.001	0.70
masturbation					
Negative attitude toward masturbation	13.03 (3.09)	13.13 (2.32)	1.91	0.167	-
Solitary sexual desire	21.59 (5.59)	19.75 (6.28)	31.96	< 0.001	0.31
Subjective orgasm experience-Affective	25.66 (4.84)	27.05 (3.85)	31.69	< 0.001	0.31
Subjective orgasm experience-Sensory	33.65 (15.74)	39.17 (15.15)	47.75	< 0.001	0.36
Subjective orgasm experience-Intimacy	7.62 (3.64)	8.19 (3.71)	12.48	< 0.001	0.15
Subjective orgasm experience-Rewards	11.34 (3.36)	11.56 (3.59)	1.82	0.177	-

Statistical analysis

A cross-sectional correlational study is proposed. First, missing values were imputed using a random forest algorithm by considering the associated variables. To examine differences in the masturbation parameters between men and women, a MANCOVA was applied for first masturbation experience (age), current solitary masturbation frequency ("Never," "Less than once a month," "Once a month," "A few times a month," "Once a week," "A few times a week," "Once a day" and "More than once a day"), negative attitude toward masturbation, solitary sexual desire and subjective orgasm experience caused by masturbation, and by taking into account these covariates: age, level of education ("Primary Education," Secondary Education" and "University degree-ongoing or completed-"), having a partner (yes or no) and frequency of prayer (similar to the masturbation frequency). Considering the differences found by sex, the subsequent analyses were presented separately for men and women. The capacity of the masturbation parameters to explain orgasm satisfaction was examined by multiple linear regression using the enter method.

The $R^{\textcircled{R}}$ environment was employed (version 3.6.3) (40) with its $RStudio^{\textcircled{R}}$ interface (version 1.2.5042) (41). For missing value imputations, the missForest package was used (version 1.4) (42). For the ordinal alpha, the Psych package was applied (version 1.9.12.31) (43). The other statistical analyses were performed with SPSS v.22.

Results

Sex differences in the masturbation parameters

The significant multivariate covariates were age [Wilk's lambda = 0.87; $F_{(8, 1,322)} = 24.49$, p < 0.001; $\eta^2 = 0.129$], having a partner [Wilk's lambda = 0.94; $F_{(8, 1,322)} = 10.91$, p < 0.001; $\eta^2 = 0.062$] and frequency of prayer [Wilk's lambda = 0.96; $F_{(8, 1,322)} = 7.42$, p < 0.001; $\eta^2 = 0.04$]. Sex had a main effect on

the masturbation parameters [Wilk's lambda = 0.77; $F_{(8, 1,322)}$ = 48.91, p < 0.001; $\eta^2 = 0.23$]. The intersubject effect on these indicators is shown in Table 2.

Regression models

For men, a significant model was obtained that explained orgasm satisfaction in sexual relationships $[F_{(9,728)}=13.01;p<0.001]$. Current solitary masturbation frequency ($\beta=-0.10$) and the Affective dimension of orgasm ($\beta=0.36$) explained 13% of variance (See Table 3). The model was also significant for women $[F_{(9,587)}=8.88;p<0.001]$ and explained 11% of orgasm satisfaction from age ($\beta=0.09$), negative attitude toward masturbation ($\beta=-0.12$), solitary sexual desire ($\beta=0.19$) and the Affective dimension of orgasm ($\beta=0.24$) (See Table 4).

Discussion

Masturbation is a sexual behavior that is contemplated to deal with sexual dysfunctions, especially orgasm difficulties (44–46). Justifying the use of masturbation in sexual therapy lies in the relation between this behavior and orgasm in sexual relationships. This is why the present study analyzes the relation between different masturbation parameters in men and women (i.e., first masturbation experience, current solitary masturbation frequency, negative attitude toward masturbation, solitary sexual desire and subjective orgasm experience) with orgasm satisfaction in sexual relationships. The results show differences between men and women in the masturbation parameters, and also in the role that these parameters play in explaining orgasm satisfaction in the sexual relationships context.

The first hypothesis is backed by significant differences between men and women in the different masturbation parameters. We observe that men's first masturbation experience took place at an earlier age than it did in women, whose finding coincides with previous studies (1, 2, 25, 30, 47).

TABLE 3 Multiple regression models for orgasmic satisfaction in men.

Predictors	В	SE	β	95% CI	t	p	R^2	VIF
Orgasmic satisfaction							0.13	
Age	0.00	0.00	0.01	-0.00, 0.01	0.03	0.974		1.23
First masturbation experience	-0.01	0.02	-0.03	-0.05, 0.02	-0.88	0.379		1.08
Current frequency of solitary masturbation	-0.10	0.04	-0.10	-0.19, -0.01	-2.22	0.027		1.79
Negative attitude toward masturbation	-0.01	0.01	-0.05	-0.04, 0.01	-1.31	0.191		1.15
Solitary sexual desire	0.01	0.01	0.08	-0.00, 0.03	1.77	0.076		1.92
Subjective orgasm experience-Affective	0.07	0.01	0.36	0.05, 0.08	7.70	< 0.001		1.85
Subjective orgasm experience-Sensory	-0.00	0.00	-0.05	-0.01, 0.00	-1.09	0.275		1.93
Subjective orgasm experience-Intimacy	0.00	0.01	0.01	-0.02, 0.03	0.32	0.746		1.70
Subjective orgasm experience-Rewards	-0.01	0.01	-0.03	-0.03, 0.01	-0.78	0.438		1.40

B, non-estandardized beta; SE, standard error; β, standardized beta; 95% CI, 95% confidence interval; VIF, variance inflation factor.

TABLE 4 Multiple regression models for orgasmic satisfaction in women.

Predictors	В	SE	β	95% CI	t	p	R^2	VIF
Orgasmic satisfaction							0.11	
Age	0.01	0.00	0.09	0.00, 0.02	2.08	0.038		1.21
First masturbation experience	0.01	0.01	0.04	-0.01, 0.02	1.01	0.314		1.10
Current frequency of solitary masturbation	-0.07	0.06	-0.07	-0.18, 0.04	-1.27	0.203		1.88
Negative attitude toward masturbation	-0.05	0.02	-0.12	-0.09, -0.01	-2.80	0.005		1.15
Solitary sexual desire	0.03	0.01	0.19	0.01, 0.05	3.43	0.001		2.11
Subjective orgasm experience-Affective	0.06	0.01	0.24	0.04, 0.09	4.91	< 0.001		1.65
Subjective orgasm experience-Sensory	-0.00	0.00	-0.03	-0.01, 0.00	-0.52	0.606		1.77
Subjective orgasm experience-Intimacy	0.00	0.01	0.01	-0.03, 0.03	0.12	0.906		1.68
Subjective orgasm experience-Rewards	-0.02	0.01	-0.08	-0.05, 0.00	-1.70	0.090		1.46

B, non-estandardized beta; SE, standard error; β , standardized beta; 95% CI, 95% confidence interval; VIF, variance inflation factor.

Traditional sexual socialization could favor more permissiveness in men and more guilty feelings associated with women practicing masturbation (48). In turn, the differences found in solitary masturbation frequency coincide with previous works in the literature, and a more frequent masturbation frequency observed for men (25, 49, 50). Attitude to the sexual double standard (i.e., the distinct evaluation made of sexual behavior depending on whether it is practiced by a man or a woman) could explain these differences given the greater sexual freedom or permissiveness that men have been traditionally conferred than women (38). Alternative considerations have also been applied to explain these differences in association with hormone levels (51).

It is worth mentioning that no differences have been found in negative attitude toward masturbation between men and women. The fact that such differences are lacking could be related to an increasingly more positive change of attitude in both men and women, as observed in other attitudes like erotophilia (52). These results contradict those recently obtained in older people and reported by Sierra et al. (30), who

indicate that men older than 50 years take a more negative attitude toward masturbation than women of a similar age. This could indicate younger generations' positive attitude toward masturbation. This question reflects the need to further study in-depth attitudes toward masturbation and the factors related to it to better understand this matter (25). Regarding differences in solitary sexual desire, the highest level found for men is consistent with previous works that report similar results (27, 28, 53, 54). This is congruent with those studies showing a close association between masturbation and solitary sexual desire (55).

On subjective orgasm experience in solitary masturbation, and in line with the results obtained by previous studies that have examined the subjective orgasm experience in the heterosexual relationships context (36, 56), women report greater intensity than men, except on the Reward dimension, which has also been shown for the gay population (57). To explain differences in orgasm intensity between men and women, women have been proposed to better localize orgasms anatomically (56), which would be associated with perceiving greater intensity (58). It has

also been indicated that women could have a bigger repertoire to describe their orgasm sensations (57, 59). Regarding the differences in their dimensions, not finding discrepancies would be expected on the Rewards dimension, which is made up of the items "peaceful," "relaxing," and "soothing," because both men and women have pointed out that relaxing is one of the main reasons to masturbate (13, 60, 61).

Regarding our second hypothesis, orgasm satisfaction in the sexual relationships context is explained in both men and women by some masturbation parameters. In the model for men and women, the Affective dimension of the subjective orgasm experience during masturbation significantly and positively explains orgasm satisfaction in the sexual relationships context. Former findings stress the importance of the Affective dimension of the subjective orgasm experience for the sexual relationships context, especially for women (62). So it might seem logical to think that this could be the case in the masturbation context where this dimension is more important for explaining orgasm satisfaction in sexual relationships.

Apart from the orgasm Affective dimension in the men's model, higher solitary masturbation frequency is also associated with lower orgasm satisfaction. These results might appear to contradict works that have described how frequency is associated with more consistent orgasms (7). However, in line with previous studies (30, 52), this association might be explained by the compensatory model of masturbation; that is, masturbation serving as a substitute of unsatisfactory sexual relationships. Therefore, lower orgasm satisfaction in the sexual relationships context might be expected to be compensated by higher masturbation frequency (26, 63).

In women, apart from the Affective dimension of orgasm, age and solitary sexual desire are positively associated, and attitude toward masturbation is negatively associated, with orgasm satisfaction in sexual relationships. The positive association of age would be expected because former works inform about a higher orgasm pleasure level with increasing age (18, 61). Moreover, the positive relation between sexual desire and sexual functioning has been well-described (27, 28, 64). In fact solitary sexual desire is associated with higher masturbation frequency (1, 55), which might imply more selferotic experiences and sexual self-knowledge (3). Finally, the fact that negative attitude toward masturbation is related to lower orgasm satisfaction is consistent with previous works (25, 65). This attitude has been associated with lower masturbation frequency (25), which might imply fewer opportunities for both sexual response self-knowledge and the associated pleasure points (7, 19).

Some differences between the models for men and women are worth stressing. The positive effect of age is only observed in women. This suggests that women benefit from enjoying more orgasm satisfaction as they age to a certain extent. Despite a negative association between age and orgasm capacity having been previously described (36, 66), these results are consistent

with some findings which reveal that women need time to interiorize a more positive relation with masturbation due to the stigmatization that their engagement in such behavior might imply (2). This suggests that the positive effects of masturbation could increase as women age. Besides, solitary masturbation frequency only has a significant effect on men, which falls in line with former results which point out that masturbation frequency in women is not significantly associated with orgasm outcomes (18). As higher masturbation frequency in men is associated with lower orgasm satisfaction in sexual relationships, it would be coherent to think that solitary sexual desire plays no relevant role to explain men's orgasm satisfaction. Finally, the differences observed in the models of men and women fall in line with the previous literature, which emphasizes how women's orgasm is associated with more variables than it is for men (56, 57, 67).

This study has its limitations, which must be taken into account to generalize its results. The study sample was formed by incidental non probabilistic sampling over social networks and only included the heterosexual population. The cross-sectional correlational experimental design and the performed statistical analyses do not allow for causality relations. So, it may be need longitudinal studies to have a deep approach about the relationship between masturbation and sexual relationships. Different parameters of masturbation could be taken into account in future studies, such as the duration of masturbation, the use of erotic toys, the techniques used or the consumption of pornography. Notwithstanding, the findings are believed relevant for its contribution to the study of masturbation and orgasm satisfaction in the sexual relationships context.

Conclusion

The obtained results confirm the differences between men and women in the masturbation parameters and their role to explain orgasm satisfaction in sexual relationships. The Affective dimension of the subjective orgasm experience during solitary masturbation is stressed as a common variable for both men and women to explain orgasm satisfaction in sexual relationships. More masturbation parameters associated with orgasm satisfaction are observed in women than men. These findings suggest that the relation between solitary masturbation and sexual relationships is a complex one. Masturbation in men could be a substitute for the satisfaction not achieved with orgasm in sexual relationship; in women, the negative attitude toward this behavior would be associated with lower orgasmic satisfaction, and a greater solitary sexual desire could promote more sexual self-knowledge. So it is important to consider these results to look more closely at the association between both sexual behaviors, and to further consolidate the usefulness of solitary masturbation in sexual therapy. Therefore, solitary masturbation is an available resource that should also be

promoted in the community context as it can improve the sexual health of the population.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethics Committee of Human Research of the University of Granada. The patients/participants provided their written informed consent to participate in this study.

Author contributions

The concept and design: JCS. Acquisition, analysis, interpretation of data, drafting of the manuscript, critical revision of the manuscript, and statistical analysis: JCS and OC. All authors contributed to the article and approved the submitted version.

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Conflict of interest

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Jose A. Piqueras,
Miguel Hernández University of
Elche, Spain
S. Maria Awaluddin,
Ministry of Health, Malaysia

*CORRESPONDENCE Mohd Noor Norhayati hayatikk@usm.my

[†]These authors have contributed equally to this work

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Effectiveness of school-based child sexual abuse intervention among school children in the new millennium era: Systematic review and meta-analyses

Ruhana Che Yusof^{1†}, Mohd Noor Norhayati^{1*†} and Yacob Mohd Azman^{2†}

¹Department of Family Medicine, School of Medical Sciences, Universiti Sains Malaysia, Kubang Kerian, Malaysia, ²Medical Practice Division, Ministry of Health, Level 7, Block E1, Parcel E, Federal Government Administrative Centre, Putrajaya, Malaysia

Introduction: School-based child sexual abuse intervention programs were developed to educate the school children to protect them from sexual abuse. The programs were evaluated to make sure the interventions were effective in reducing child sexual abuse cases (CSA). This review aimed to determine the effectiveness of the school-based child sexual abuse intervention programs in the new millennium era (2000–2021) in improving the knowledge, skills, and attitude of school children under 18 years old toward child sexual abuse.

Methods: A systematic search was conducted through MEDLINE (PubMed), EBSCO, and SCOPUS databases to collect full English articles related to school-based CSA intervention programs published from 2000 to 2021.

Results: A total of 29 studies from randomized control trial and quasi-experimental from several countries was analyzed. Comparisons within group of pre-post intervention for knowledge, skills, and attitude were measured by standardized mean difference (SMD) and 95% CI of -1.06 (95% CI: -1.29, -0.84), -0.91 (95% CI: -1.2, -0.61), and -0.51 (95% CI: -3.61, 0.58), respectively. Meanwhile for between intervention and control group comparisons, the SMD of knowledge was 0.9 (95% CI: 0.63, 1.18), skills was 0.39 (95% CI: 0.07, 0.71), and attitude was 1.76 (95% CI: 0.46, 3.07).

Conclusion: The programs were found to be effective in improving the knowledge, skills, and attitude of the students from pre-intervention to post-intervention and between the intervention and control groups.

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Introduction

Child sexual abuse (CSA) is associated with the risk of adverse psychosocial and health effects, resilience processes include several protective factors that can be enhanced through preventative and early intervention efforts (family support, parent-child relationships, social support, etc.) (1). The World Health Organization has classified

CSA as "the involvement of a child in sexual activity that he or she does not fully comprehend, is unable to give informed consent to, or for which the child is not developmentally prepared and cannot give consent, or that violate the laws or social taboos of society" (2).

A previous review (3), had reported the definition of child sexual abuse can be found in the perspective of child protection (ensuring a child's safety), criminal (securing prosecutions), and clinical (the impact of abuse on the child) (4) and classified an act of abuse into three levels which are noncontact, contact, and penetrative abuse. The review also mentioned more recent definitions by a study (5) that incorporate what were seen as recent developments (e.g., peer abuse, child prostitution, internet pornography, pedophile networks, and grooming over the internet), in addition to traditional categories such as incest.

However, the term "child sexual abuse" is defined differently by epidemiological studies, policy documents, and legal frameworks that use different approaches to the composition of the CSA, the definition of the acts that make up the CSA, and the nature of consent. The study developed a conceptual model to classify CSA. According to the model, CSA required the presence of all four factors: (i) the person must be a child; (ii) true consent must be absent; (iii) the acts must be sexual; (iv) the acts must constitute abuse. These definitions of CSA and abuse distinguish the overall idea of CSA from others like assault, harassment, and victimization, and the model demonstrates when and why an act or experience is more properly characterized as CSA (6).

In order to prevent CSA, many intervention programs were made globally. Educate young children on CSA is one approach in the intervention program with assumptions that children can (i) recognize the characteristics of an exploitative or abusive encounter, touch, engagement, or scenario; (ii) psychologically oppose an abuser's threats or manipulations; (iii) defy the authority of an adult; (iv) refuse to accept the abuser's affection, attention, and/or material rewards; (v) be willing to disclose abuse perpetrated by others (7).

The fundamental purpose of CSA intervention efforts has been to change children's knowledge and skills through group-based personal safety instruction, which is frequently offered in educational settings (8). School-based programs can be implemented universally at a minimal cost without stigmatizing people at higher risk, program content corresponds with school health curricula, and schools serve as a direct link to additional preventative targets such as school staff, parents, relatives, and communities (9).

A selection of intervention programs that achieved four or more outcome improvements (e.g., knowledge, skills, emotions, disclosure, and maintenance of gains) was used to identify the essential characteristics of effective intervention programs (3) such as improved conceptual knowledge of sexual abuse (remembering), enhanced detection of likely sexual abuse circumstances (recognition), increased personal safety skill knowledge and sensation of security over personal body

area (resisting), and potential and occurrence of disclosures (reporting) (10).

The main focus of school-based CSA programs is to reduce the risk of child abuse by teaching children child abuse-related knowledge and self-protection skills (11). Beyond that, these programs also improved the behavior of participants as well as a positive attitude regarding CSA (12). Thus, this study aimed to review the effectiveness of the school-based CSA intervention programs which specifically focus on CSA on knowledge, skills, and attitude of students under 18 years old in reducing risks of child abuse.

Methods

Types of studies

The effectiveness of school-based CSA intervention programs among school students under the age of 18 was evaluated by a systematic review and meta-analysis of research. The outcome measures involved knowledge, skills, and attitude of the children on CSA. The studies were reviewed using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (13).

Search methods

A systematic search was conducted to identify relevant articles to include in the review. Databases involved were MEDLINE (PubMed), EBSCO, and SCOPUS based on the search terms "[(school-based) AND (prevention OR intervention)] AND (sexual abuse)." All studies published from the year 2000 to 22 February 2022 were extracted to determine their eligibility for inclusion in this review. The search was limited to full-text articles written in English and the age limit was 18 years old and below. The reference lists of included citations were cross-checked to locate other potentially acceptable research.

Study selection

All the records found by the search approach were exported to EndNote X8 software (Clarivate Analytics, Philadelphia, PA). Duplicate articles were removed. The automation tool using terms (review) or (prevalence) or (protocol) or (qualitative) or ("meta-analysis") or ("case report") was used to remove irrelevant studies by the methodologies. Meanwhile, terms (community) or (alcohol) or (drug) or ("substance use") or (smoking) or (suicidal) or (HIV or AIDS) or (bullying) or (trauma) or (dating) were used to remove irrelevant studies by the interesting outcome. The titles and abstracts of the identified

papers were checked by two independent reviewers (RCY, MNN). To assess their eligibility, the full texts of eligible papers were obtained and thoroughly examined. After a consensus discussion, a third reviewer (YMA) was consulted in the event of a conflict between the two reviewers. The search approach was depicted in the PRISMA flow chart, which included and excluded studies as well as the grounds for exclusion.

Data extraction and management

The extracted data were entered into Microsoft Excel (Microsoft Corporation, Redmond, WA). The data included the first author, year of publication, study location, study design, study population, sample size, name of the intervention program, tools, outcome measures, and data to generate effect estimates if plausible. The studies with incomplete data were excluded from the review. This review was focused on school children aged under 18 years old with the programs specifically on child sexual abuse only. The interest outcomes of knowledge, skills, and attitude on CSA were measured in this review.

Assessment of risk of bias

Risk of bias assessment for data quality was performed using the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) version of 22 August 2019 (14) and Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I) (15). Independent bias assessments were carried out by two reviewers (RCY, MNN).

Measures of treatment effect

The evaluation of the program's effects was reported in pooled standardized mean differences (SMD) of the outcomes (knowledge, skills, and attitude) with a 95% CI. The SMD was used when the studies assess the same outcome but measure it with different tools or scales. The evaluation involved the pre- and post-intervention that measures within-group and comparison between the intervention and control groups that measures between-group effect. Subgroup analysis was done when applicable.

Data synthesis

Studies with the randomized control trial (RCT) or quasiexperimental pre-post trial were selected to include in the review. Measurement of outcomes between pre- and postintervention (within-group), and between intervention and control groups (between-group) were extracted from the studies and were recorded in Microsoft Excel (Microsoft Corporation, Redmond, WA).

For pre-post intervention outcome, mean and pooled standard deviation (SD) was used to calculate the SMD for within-group comparison. Meanwhile, for comparison between intervention and control groups, mean difference (MD) and SD_{pooled} of within-group outcome from each group were used to calculate the SMD of between-group comparison. The SMD used the Hedge' g formula to determine pooled intervention-specific SDs as follows:

$$Hedge'g = \frac{MD}{SD_{pooled}},$$
 where
$$SD_{pooled} = \sqrt{\frac{SD_1^2 + SD_2^2}{2}}.$$

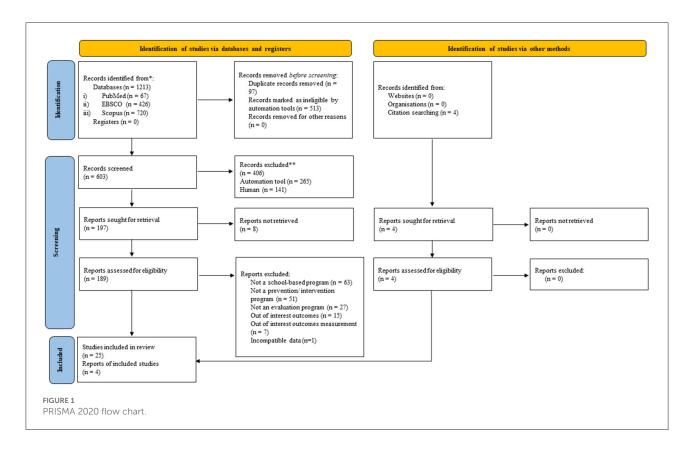
Individual study SMDs are weighted before being aggregated in meta-analysis.

The analysis was performed with Review Manager software version 5.4 (Nordic Cochrane Centre, Copenhagen, Denmark). This software used a Hedges' g formula to calculate SMD. The SMD values range between 0.2 and 0.5 and are regarded as small, values between 0.5 and 0.8 are considered medium, and values >0.8 are considered large (16). Continuous data using generic inverse variance with a random-effects model was applied to pool the effect size by the SMD of the studies' data. The heterogeneity was assessed by I^2 statistic and used the guide as outlined: 0-40% might not be important; 30-60% may represent moderate heterogeneity; 50-90% may represent substantial heterogeneity; 75-100% would be considerable heterogeneity (17). Subgroup analysis was performed based on study designs (RCT and quasi-experimental), school levels (preschool, primary, and secondary), and children's abilities (normal children and children with disability). If there was a possibility of publication bias, a visual assessment of funnel plots and statistical analysis by Egger's test was used. Sensitivity analysis was done to assess outliers in the synthesized results. We assessed the quality of evidence for the outcomes according to the GRADEpro methodology (18) for risk of bias, inconsistency, indirectness, imprecision, and publication bias; classified as very low, low, moderate, or high.

Results

Study selection

A total of 1,217 studies were identified through the primary search databases and secondary citations. However, 610 studies were removed due to duplicates and were marked as ineligible by automation tools. After screening and retrieving, 189 studies including four studies from citation search were assessed for eligibility. After the assessment, a total of 30 studies met the inclusion and exclusion criteria. However, one study (19) was



excluded due to incompatible data and finally, only 29 studies were decided to be included in the review (Figure 1).

Study characteristics

The included studies were published from the year 2000 to 2021 in the United States (eight studies), Turkey (five studies), Korea (four studies), China (three studies), Germany (three studies), Canada (two studies), and one study each from Spain, Ecuador, Pakistan, and Thailand.

The studies involved 14,817 school children from preschool level (20, 21), primary/elementary school level (23 studies) including a study in special schools for deaf and hard of hearing children, and secondary school level (22, 23). One study was done at both primary and secondary levels (24) and one study was done in a school for children with developmental delays and disorders involving children aged 10 years old to 15 years old (25).

A total of eight studies used RCT as a study design (22, 23, 26–31), and 21 studies by quasi-experimental (20, 21, 24, 25, 32–48). Evaluation of the school-based CSA intervention programs involved the evaluation of knowledge (24 studies), skills (13 studies), and attitude (3 studies) toward CSA. The characteristics of the included studies were summarized in the Supplementary Table 1.

In this new millennium era, some of the intervention programs in this review were developed using new technologies such as web-based and smartphone-based applications (38, 41) since this function is user-friendly due to multi-platform development and can be accessed anytime and anywhere. In 2005, a study in Korea (23) evaluated a CD-ROM-based educational program to increase knowledge of CSA because of its capability to combine audio, visual, and interactive capabilities, and the ability to store text, graphics, images, and movies in a tiny drive. However, in school-based intervention programs, passive teaching strategies such as video, lecture, and workshops, as well as active teaching techniques such as role-playing, modeling, and rehearsing (27, 33), are still used.

Most of the studies in this review measured the outcomes using well-known questionnaires whether in original form or revised or modified versions such as the "Children's Knowledge of Abuse Questionnaire" (CKAQ), the "Personal Safety Questionnaire" (PSQ), "What If" Situation Test (WIST), and the "Body Safety Training Program (BST)." Some of the studies (38, 39, 48) developed new validated questionnaires to measure the outcomes of the studies. The other studies adapted and/or modified the well-known curriculum tools such as the "Good Touch Bad Touch Curriculum Test" (33, 44), "Play it Safe!" (30), "Florida Child Safety Matters[®] (CSM) evaluation (31), questionnaire of "Sexuality Knowledge Level" (20) and WHO life skills development concepts questionnaires (24).

Risk of bias assessment

Data quality assessment for risk of bias was performed using the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) checklist (14) in eight RCT studies. Meanwhile, the risk of bias assessment by Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) checklist (15) was used in 21 quasi-experimental studies. The overall risk of bias was classified as low risk after the assessment for all the items by two reviewers (RCY, MNN) in both checklists (Supplementary Tables 2, 3).

Outcomes and subgroup analyses

Table 1 summarized the findings for knowledge, skills, and attitude outcomes for within-group (pre-post intervention) comparison, subgroup analysis by study designs for knowledge outcome, and subgroup analysis by types of children for skills outcome performed. For between-group (intervention and control groups) comparison, subgroup analysis by school levels for knowledge outcome was performed. Subgroup analyses for other outcomes were not performed due to the limited number of studies.

Knowledge

The within-group comparison showed that the CSA intervention programs increased knowledge levels in school children compared to pre-intervention [SMD: -1.06 (95% CI: -1.29, -0.84); $I^2 = 97\%$; p-value < 0.00–1; 24 studies; 20,022 participants] (Table 1) with the SMDs ranging from -0.13 to -7.64 (Supplementary Figure 1).

Subgroup analysis was done by study designs. The knowledge levels in studies with RCT design [SMD: -0.44 [95% CI: $-0.58,\,-0.31$]; $I^2=81\%;\,p\text{-value}<0.001;$ seven studies; 6,737 participants; high quality evidence] and quasi-experimental design [SMD: -1.43 (95% CI: $-1.78,\,-1.07$); $I^2=97\%;\,p\text{-value}<0.0001;$ 17 studies, 13,332 participant; high quality evidence] (Figure 2, Supplementary Table 4) increased in post-intervention compared to pre-intervention. Heterogeneity was considerable in this subgroup analysis. Large effect size was showed in quasi experimental group but medium effect size in RCT group.

Meanwhile, for between-groups comparison, the CSA knowledge levels were increased in the intervention group compared to the control group [SMD: 0.9 (95% CI: 0.63, 1.18); $I^2=97\%$; p-value<0.0001; 20 studies; 8,740 participants; high quality evidence] with considerable heterogeneity and large effect size. The SMDs range from -0.33 to 5.06 (Supplementary Figure 2, Supplementary Table 5).

Subgroup analysis by school levels were done for between-group comparison. Subgroup analysis of knowledge levels by, showed that the SMD for preschool were 3.08 [(95% CI: -0.72,

6.89); $I^2 = 98\%$; p-value < 0.0001; two studies; 208 participants; high quality evidence], for primary school were 0.85 [(95% CI: 0.51, 1.18); $I^2 = 97\%$; p-value < 0.0001; 15 studies; 7,090 participants; high quality evidence], and for secondary school were 0.28 [(95% CI: -0.4, 0.95); $I^2 = 33\%$; p-value = 0.22; two studies; 912 participants; high quality evidence], (Figure 3, Supplementary Table 5). SMD of 15 studies at primary school level showed a large effect size. Considerable heterogeneity was observed in this subgroup analysis.

Skills

Within-group comparison showed that the CSA intervention programs increased skills levels among school children in post-intervention compared to pre-intervention [SMD: -0.91 (95% CI: -1.2, -0.61); $I^2=93\%$; p-value < 0.0001; 12 studies; 4,632 participants; Table 1] with large effect size. The SMDs range from -0.14 to -7.64 (Supplementary Figure 3).

Subgroup analysis was done for the type of children in skills outcome. The skills levels was increased in post-intervention compared to pre-intervention in school children with normal ability [SMD: -0.76 (95% CI: -1.04, -0.49); $I^2=93\%$; p-value<0.0001; 10 studies; 4,510 participants; high quality evidence] and in school children with disability [SMD: -4.27 (95% CI: -10.69, 2.15); $I^2=98\%$; p-value<0.0001; two studies; 156 participants; high quality evidence; Figure 4, Supplementary Table 4]. The effect size for children with normal ability was considered medium. Considerable heterogeneity was presented in this subgroup analysis.

Meanwhile, between-group comparison showed that the skills levels of CSA were increased in the intervention group compared to the control group [SDM: 0.39 (95% CI: 0.07, 0.71); $I^2=95\%$; p-value <0.0001; 13 studies; 4,638 participants; Table 1] with considerable heterogeneity and medium effect size. The SMDs range from -1.84 to 3.04 (Supplementary Figure 4). Subgroup analysis was not done for this comparison since the effect size of this outcome was small (SMD <0.5) compared to the other outcomes in which the effect sizes were more than 0.9.

Attitude

Within-group comparison of attitude showed that the attitude levels were increased in post-intervention compared to pre-intervention, but the difference was not significant [SMD: -0.51 (95% CI: -3.61, 0.58); $I^2 = 97\%$; p-value < 0.0001; two studies; 158 participants; high quality evidence; Supplementary Figure 5, Supplementary Table 4] considerable heterogeneity.

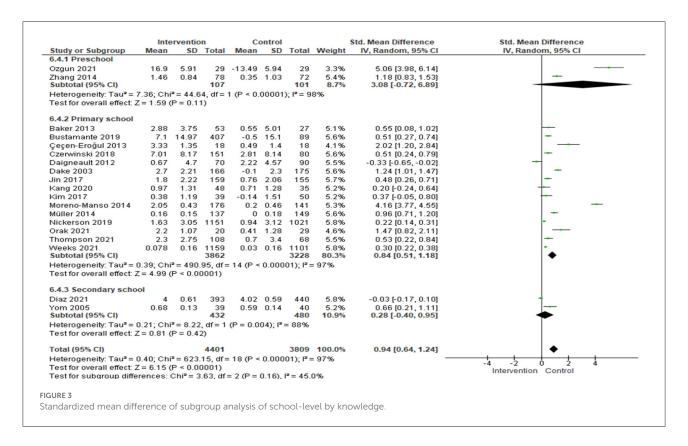
For between-group comparison, the CSA intervention programs increased the attitude level in the intervention group compared to the control group [SMD: 1.76 (95% CI:

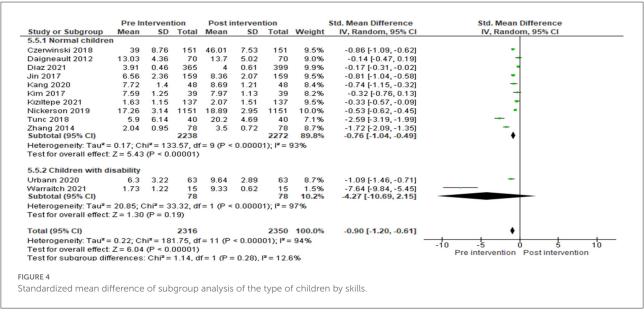
TABLE 1 Comparisons, outcomes, and subgroup analyses.

Comparison	Outcome	Subgroup	Studies	N	SMD (95% CI)	I^{2} (%)	<i>p</i> -value	I^2 diff (%)	<i>p</i> -value
Within group	Knowledge		24	20,022	-1.06 (-1.29, -0.84)	97	< 0.0001		
		Study design							
		RCT	7	6,737	-0.44 (-0.58, -0.31)	81	< 0.0001		
		Quasi	17	13,332	-1.43 (-1.78, -1.07)	97	< 0.0001		
		Total	24	20,069	-1.06 (-1.29, -0.84)	97	< 0.0001	96.1	< 0.0001
	Skills		12	4,632	$-0.91 \ (-1.20, -0.61)$	94	< 0.0001		
		Types of children							
		Normal	10	4,510	-0.76 (-1.04, -0.49)	93	< 0.0001		
		With disability	2	156	$-4.27 \; (-10.69, 2.15)$	98	< 0.0001		
		Total	12	4,666	$-0.90 \ (-1.20, -0.61)$	94	< 0.0001	7.0	0.300
	Attitude		2	158	-1.51 (-3.61, 0.58)	97	< 0.0001		
Between group	Knowledge		20	8,740	0.90 (0.63, 1.18)	97	< 0.0001		
		School level							
		Preschool	2	208	3.08 (-0.72, 6.89)	98	< 0.0001		
		Primary school	15	7,090	0.84 (0.51, 1.18)	97	< 0.0001		
		Secondary school	2	912	0.28 (-0.40, 0.95)	33	0.22		
		Total	19	8,210	0.94 (0.64, 1.24)	97	< 0.0001	45.1	0.160
	Skills		13	4,638	0.39 (0.07, 0.71)	95	< 0.0001		
	Attitude		3	342	1.76 (0.46, 3.07)	96	0.0002		

n, number of samples; SMD, standardized mean difference; CI, confidence interval; $\rm I^2, I$ squared.

	Pre I	nterven	tion	Post	interven	tion		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
5.4.1 RCT									
Bustamante 2019	61.9	14.1	407	69	15.8	407	4.8%	-0.47 [-0.61, -0.33]	•
Daigneault 2012	13.03	4.36	70	13.7	5.02	70	4.4%	-0.14 [-0.47, 0.19]	+
Diaz 2021	3.91	0.46	393	4	0.61	440	4.8%	-0.17 [-0.30, -0.03]	•
Nickerson 2019	17.26	3.14	1151	18.89	2.95	1151	4.8%	-0.53 [-0.62, -0.45]	•
Thompson 2021	8.1	2.8	108	10.4	2.7	108	4.5%	-0.83 [-1.11, -0.56]	-
Weeks 2021	0.704	0.158	1195	0.782	0.156	1159	4.8%	-0.50 [-0.58, -0.41]	•
Yom 2005	0.62	0.13	39	0.68	0.13	39	4.1%	-0.46 [-0.91, -0.01]	.
Subtotal (95% CI)			3363			3374	32.3%	-0.44 [-0.58, -0.31]	•1
Heterogeneity: Tau² = 0.0	2; $Chi^2 = 3$	32.27, df	= 6 (P <	0.0001)	$ ^2 = 81$	%			
Test for overall effect: Z =	6.53 (P <	0.00001)						
5.4.2 Quasi experimenta									
Baker 2013	18.06	3.63	53	20.94	3.87	53	4.2%	-0.76 [-1.16, -0.37]	-
Cecen-Eroğul 2013	5.33		18	8.66	1.28	18	2.8%	-2.42 [-3.30, -1.54]	
Chamroonsawasdi 2010				26.32	2.87	313	4.8%	-0.13 [-0.29, 0.02]	4
Czerwinski 2018	39		151		7.53	151	4.6%	-0.86 [-1.09, -0.62]	•
Dake 2003	9.6		166	12.3	2	166	4.6%	-1.22 [-1.45, -0.98]	•
Edwards 2020	0.72	0.154	48	0.78	0.118	48	4.2%	-0.43 [-0.84, -0.03]	+
Jin 2017	6.56		159	8.36	2.07	159	4.6%	-0.81 [-1.04, -0.58]	•
Kang 2020	7.72		48	8.69	1.21	48	4.2%	-0.74 [-1.15, -0.32]	+
Kim 2017	7.59	1.25	39	7.97	1.13	39	4.1%	-0.32 [-0.76, 0.13]	-
Moreno-Manso 2014	0.2	0.41	176	2.25	0.44	176	4.2%	-4.81 [-5.22, -4.40]	-
Müller 2014	0.63	0.16	137	0.79	0.14	137	4.6%	-1.06 [-1.31, -0.81]	+
Orak 2021	7.35	1.42	20	9.55	0.51	20	3.1%	-2.02 [-2.80, -1.25]	
Ozgun 2021	18.96	5.4	29	35.86	6.38	29	3.2%	-2.82 [-3.56, -2.08]	
Smothers 2011	86.4	8.64	132	92.24	9.17	132	4.6%	-0.65 [-0.90, -0.41]	-
Tutty 2020	6	2.5	5084	8.3	2	5084	4.9%	-1.02 [-1.06, -0.97]	•
Warraitch 2021	1.73	1.22	15	9.33	0.62	15	0.9%	-7.64 [-9.84, -5.45]	
Zhang 2014	2.04	0.95	78	3.5	0.72	78	4.3%	-1.72 [-2.09, -1.35]	÷
Subtotal (95% CI)			6666			6666	67.7%	-1.43 [-1.78, -1.07]	♦
Heterogeneity: Tau² = 0.4 Test for overall effect: Z =				P < 0.00	001); I²=	97%			
Total (95% CI)			10029			10040	100.0%	-1.06 [-1.29, -0.84]	•
Heterogeneity: Tau² = 0.2 Test for overall effect: Z = Test for subgroup differei	9.35 (P <	0.00001)					,	Pre intervention Post intervention
URE 2									





0.46, 3.07); $I^2 = 96\%$; %; p-value = 0.0002; 3 studies; 342 participants; high quality evidence; Supplementary Figure 6, Supplementary Table 5] considerable heterogeneity. Both models showed considerable heterogeneity. Subgroup analysis was done on this outcome due to a small number of studies.

Publication bias

Funnel plot asymmetry was observed in within-group and between-group for knowledge and skills outcomes (Supplementary Figures 7–13). For within-group comparison, the Egger's tests were not significant in CSA knowledge levels

(p-value = 0.583) and in study designs assessment (p-value = 0.581) but significant in skills levels (p-value = 0.043) and type of children (p-value = 0.042).

Meanwhile for between-group comparison, the Egger's tests were significant in knowledge levels (p-value = 0.012) and school levels (p-value = 0.014) but not significant in skills levels (p-value = 0.58). Publication bias was not assessed for attitude outcome due to a limited number of studies.

Outlier and sensitivity analysis

Finally, one study (25) was detected as an outlier because its values were beyond the range of values compared to other studies. It was included in the within-group analyses of knowledge levels, subgroup analyses of quasi-experimental (study design) and skills levels, and in the subgroup of children with disability (type of children).

Sensitivity analysis for the within-group comparison for skills levels outcome showed a change in the pooled estimate of SMD from -6.6 (95% CI: (-17.66, 4.47) to -1.09 (95% CI: (-1.46, -0.71) for children with disability. There were no differences in the effect estimates for within-group for knowledge levels, within-group comparison of study design subgroup for the quasi-experimental and total subgroup, within-group skills levels, and the total subgroup of type of children (Table 2).

Discussion

This review found that the school-based CSA intervention programs from various studies between the year 2000 to 2021 were effective in increasing knowledge, skills, and attitude toward CSA among school children aged under 18 years old. Further explorations by subgroup analyses found that the SMDs were higher quasi-experimental for study design, and in children with disability in the type children. At the school level, preschool children had the highest SMD compared to primary and secondary school children which indicates the age difference in knowledge levels following the CSA intervention programs. However, the conclusion should be made cautiously due to the heterogeneity in the analyses.

The most often assessed study outcome on the effectiveness of the CSA intervention programs was knowledge acquisition, either through questionnaires aimed to capture factual knowledge or through vignettes that attempted to determine applied knowledge (49). In this review, all studies showed an increasing knowledge of CSA after the intervention programs. A meta-analysis showed that the CSA intervention programs gained factual and applied knowledge as early up to two weeks after the intervention. Older children appeared to gain better knowledge than younger children using questionnaire-based

measures compared to vignette-based measures (49). A review reported that preschool children had a larger increase in CSA knowledge than elementary and middle school students (50). However, we found no difference in CSA knowledge in preschool, primary and secondary schools. Considerable heterogeneity was present with only two studies representing preschool level and secondary school level. A large effect size was also presented in the overall school-level model. A recent review reported that CSA-related knowledge had a significant overall effect with a medium effect size on school-based CSA intervention programs after controlling the moderating effects of samples, study designs, and program characteristics by two three-level meta-analyses (51).

Subgroup analyses by study design reported medium effect size in seven RCTs and large effect size in 17 quasi-experimental studies. A well-designed RCT provided strong evidence of a cause-effect relation in evaluating the intervention and the study design was also capable of determining the validity and generalizability of the findings (52) compared to quasi-experimental. A quasi-experimental of nonrandomized study or pre-post intervention study was chosen due to the small availability of participants in the included studies. Eleven quasi-experimental studies in our review had less than 100 sample sizes. Other reasons for the use of this design are when randomization is not allowed for known efficacy intervention and difficulty in randomizing the participants and the locations (53).

The CSA intervention programs also evaluated the skills of children. The differences were seen in both comparisons, prepost intervention and between intervention and control group. The effect on skills was similar to a review in China (50). Generally, the important components of self-protection skills that are included in intervention programs were to disclose abuse, recognized risk situations, deal with emotions, get away and find help, assertiveness skills to say "no," and increase self-esteem (54). The likelihood of sexual abuse is higher in children with disability compared to normal children and higher in certain types of disabilities such as mental or intellectual disability (55). The effectiveness of intervention programs for children with intellectual disabilities should be adapted based on the needs of the children and learning styles such as simplifying words or symbolic communication such as pictures, images, symbols, and signs with more repetition since the children are known to have lacked in verbal skills (56).

Evaluation of attitude or perception or belief was one of the components in evaluating a CSA intervention program. A good positive attitude toward personal safety is required to face sexual abuse (46) and all the involved studies in this review showed increased attitudes towards child sexual abuse both within and between groups comparisons. A review (57) stated that the participants used the knowledge and skills they had gained from the intervention programs in specific real-life circumstances and were able to help friends with the information

TABLE 2 Sensitivity analysis for an outlier study (25).

Comparison	Outcome	Subgroup	N studies	Pooled estimate with outlier SMD ^a (95% CI)	I ² (%)	N studies	Pooled estimate without outlier SMD ^a (95% CI)	I ² (%)
Within group	Knowledge		24	-1.06 (-1.29, -0.84)	97	23	-1.01 (-1.22, -0.79)	97
		Study design						
		Quasi	17	-1.43 (-1.78, -1.07)	97	16	-1.31 (-1.65, -0.96)	97
		Total	24	-1.06 (-1.29, -0.84)	97	23	-1.01 (-1.22, -0.79)	97
	Skills		12	-0.87 (-1.17, -0.57)	94	11	-0.77 (-1.04, -0.51)	93
		Type of children						
		With disability	2	-6.6 (-17.66, 4.47)	98	1	-1.09(-1.46, -0.71)	NA
		Total	12	-0.87 (-1.16, -0.57)	94	11	-0.79 (-1.06, -0.53)	93

^aStandardized mean difference.

(58) The attitude toward sexual abuse may influence children's behavior and the ability of a person to respond to the sexual abuse (59). The greater impact, especially for preschool children may be achieved by integrating entertainment, such as videos, songs, and picture books in the intervention programs (28). It potentially improved the attitude of the children toward sexual abuse (60).

Funnel plot asymmetry should not be confused with publication bias because it might have a variety of other reasons (61). The asymmetry shapes of funnel plots in this review were believed to arise from the heterogeneity of the study. One approach to account for heterogeneity is assuming that heterogeneity is random by a random-effect model. Asymmetry or unusual shapes in funnel plots can be caused by heterogeneity, reporting bias, or chance (61). Asymmetry of funnel plots was measured by Egger's test which is based on regression intercept. Egger's test reports the *p*-value of the regression but not the magnitude of the intercept due to difficulty in providing a severity range of publication bias (62). Publication bias is difficult to assess in reviews of 10 or fewer studies due to a lack of power and in reviews of non-randomized studies due to confounding concerns (63).

This review had limitations. This review did not apply meta-regression in the analysis. No mediator or moderator effect was analyzed. On the other hand, a study in China showed the mediator effect of attitude towards messages from picture books that mediated the message framing on refusal skills. This in turn inspired participants to apply the refusal skills learned from the messages (28). This review also focused only on CSA and did not include physical abuse, emotional abuse, and neglect. The search was limited to publications published in English exclusively which may have reduced the generalization of this review. Limited database search can introduce publication bias. However, MEDLINE was determined to be the best single source for retrieving a systematic review, with an 89.7% inclusion of free and open-access papers (64). However, it is also advised to do a thorough search for research

utilizing multiple databases to decrease potential biases in the included studies.

Conclusion

The school-based CSA intervention programs held from the year 2000 to 2021 in the new millennium era were reported to increase the knowledge, self-protection skills, and attitude toward CSA among school children under 18 years old. The improvement in the key components of CSA intervention programs indicated that the programs were effective. However, it was not proven to reduce the risk of CSA since this review did not study the prevalence of CSA in this duration.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

RCY and MNN: conceptualization, methodology, and validation. RCY: software, formal analysis, data curation, and writing—original draft preparation. MNN and YMA: writing—review and editing. MNN: visualization and supervision. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The reviewer SA declared a shared affiliation with the author YMA to the handling editor at the time of review.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh. 2022.909254/full#supplementary-material

SUPPLEMENTARY FIGURE 1

Standardized mean difference of within-group intervention by knowledge.

SUPPLEMENTARY FIGURE 2

Standardized mean difference of between-group intervention by knowledge.

SUPPLEMENTARY FIGURE 3

Standardized mean difference of within-group intervention by skills.

SUPPLEMENTARY FIGURE 4

Standardized mean difference of between-group intervention by skills.

SUPPLEMENTARY FIGURE 5

Standardized mean difference of within-group intervention by attitude.

SUPPLEMENTARY FIGURE 6

Standardized mean difference of between-group intervention by attitude

SUPPLEMENTARY FIGURE 7

Funnel plot of within-group comparison by knowledge.

SUPPLEMENTARY FIGURE 8

Funnel plot of study design by knowledge.

SUPPLEMENTARY FIGURE 9

Funnel plot of within-group comparison by skills.

SUPPLEMENTARY FIGURE 10

Funnel plot of type of children by skills.

SUPPLEMENTARY FIGURE 11

Funnel plot of between-group comparison by knowledge.

SUPPLEMENTARY FIGURE 12

Funnel plot of school level by knowledge.

SUPPLEMENTARY FIGURE 13

Funnel plot of between-group comparison by skills.

SUPPLEMENTARY TABLE 1

Characteristics of the included study.

SUPPLEMENTARY TABLE 2

Assessment risk of bias by ROB-2.

SUPPLEMENTARY TABLE 3

Assessment risk of bias by ROBINS-I.

SUPPLEMENTARY TABLE 4

The quality of evidence for the within-group comparison according to GRADEpro methodology.

SUPPLEMENTARY TABLE 5

The quality of evidence for the between-group comparison according to GRADEpro methodology.

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Francisco Rivera,
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REVIEWED BY

Ravi Philip Rajkumar, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), India Deepa K. Damodaran, Jain University, India Hao Zhou, Guizhou Provincial People's Hospital, China

*CORRESPONDENCE Junfen Fu fjf68@zju.edu.cn Rongwang Yang colortea@zju.edu.cn

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Mental health status of children with disorders of sexual development and their correlates

Jingjing Cai¹, Guochun Zhu¹, Hongjuan Tian², Jinna Yuan³, Huihui Gao⁴, Liying Sun⁴, Guanping Dong³, Wei Ru², Dehua Wu², Daxing Tang², Weijia Gao¹, Junfen Fu^{3*} and Rongwang Yang ¹⁰ 1*

¹Department of Child Psychology, Children's Hospital, National Clinical Research Center for Child Health, Zhejiang University School of Medicine, Hangzhou, China, ²Department of Urology, Children's Hospital, National Clinical Research Center for Child Health, Zhejiang University School of Medicine, Hangzhou, China, ³Department of Endocrinology, Children's Hospital, National Clinical Research Center for Child Health, Zhejiang University School of Medicine, Hangzhou, China, ⁴Department of Pediatrics and Adolescent Gynecology, Children's Hospital, National Clinical Research Center for Child Health, Zhejiang University School of Medicine, Hangzhou, China

Disorders of sexual development (DSD) refer to the congenital abnormalities of chromosomes, gonads, or gender anatomy. Children with DSD usually experience more stress. The present study aims to evaluate the mental health status of children with DSD, and to explore the potential relevant factors. We included 30 children with DSD and 30 age- and gender-matched children without DSD as the control group. All the children and their parents completed the scales of the Hamilton Anxiety Scale (HAMA). Children over 8 years old (n = 22) completed the Screen Scale for Child Anxiety Related Emotional Disorders (SCARED), the Depression Self-rating Scale for Children (DSRSC), and the Egna Minnen av Barndoms Uppfostran-own memories of parental rearing practices in childhood. DSD children had significantly higher somatic anxiety, mental anxiety, and total anxiety scores than the control group (p < 0.001). The scores of the SCARED, anxiety, and depression subscales of DSD children were higher than those of control children (p < 0.05 and p < 0.001, respectively). The correlation analysis showed that the score of generalized anxiety was positively related to age and entertainment. The regression analysis showed that age was a major factor that affected generalized anxiety in DSD children, and neuroticism was a major factor of anxiety disorder and separation anxiety in DSD children. Children with DSD have obvious anxiety problems, which are associated with family environmental factors (entertainment, success, and conflicts) and age. It is important to focus emphasis on emotional stability in children with DSD for detecting anxiety-related emotional disorders early.

KEYWORDS

disorders of sexual development, anxiety, parental rearing practices, family environment, mental health

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Introduction

Disorders of sexual development (DSD) are a group of disorders classified by congenital abnormalities of chromosomes, gonads, or gender anatomy, mostly seen in newborns and adolescents (1–3). DSDs have a wide spectrum, and patients with different pathophysiological changes present with different clinical manifestations (1–3). Newborns with DSDs normally present with genital abnormalities, while adolescents with abnormal sexual development present during youth development (4). DSDs are divided into three categories: 46, XX (mainly related to SRY gene translocation, androgen excess), 46, XY (mainly related to gao differentiation development, androgen synthesis, and utilization disorders), and sex chromosome DSD (mainly related to sex chromosomal karyotype abnormalities) (1–5).

Children and adolescents with DSDs are at high risk of emotional problems. The relevant factors affecting emotional problems mainly focus on three aspects: genetic factors, psychological factors, and social environmental factors.

Ediati A et al. (6) compared 118 Indonesian DSD patients aged 6-41 years (60 children, 24 adolescents, and 34 adults) with 118 healthy control subjects matched for age, gender, and residential settings. The results of the Child Behavioral Checklist (CBCL) showed that parents of DSD children had significantly more emotional and behavioral problems than those of normal children. The results of the Adult Self-Report (ASR) indicated that adults with DSD had significantly more internalizing problems, particularly anxiety and depression, than the control group. The research suggested that Indonesian patients with DSD who had not been treated for most of their lives suffered from more emotional and behavioral problems than matched controls. Kleinemeier E et al. (7) studied 60 DSD teenagers aged 13-16 years old using standardized instruments and scales covering health-related quality of life, mental health, physical image, and other issues related to sexual behavior and response to DSDs. Compared to adolescents who entered puberty spontaneously, those who needed hormonal treatment to induce puberty have been reported to be affected in nearly all outcomes. It has been reported that girls with DSDs have less sexual activity than female controls.

It is stated that children with these disorders have high levels of stress. The timing of diagnosis seems to specifically contribute to the increased risk of developing negative feelings, intense reactions, or acute psychological conditions (8). These children may face confusion about how to accept and adapt to the opposite sex lifestyle, especially self-identity regarding body image. They would worry or even fear using the toilet in public. Children might have little idea how to live with peers of the same age with a new gender since they are afraid of too much attention from others. The individuation process of adolescence and its

close relationship with peer identification increase the sensibility toward the pressure of normality or conformity (5).

Children may find it difficult to explain DSDs to their classmates and teachers, which might hinder the development of their social behavior (5). Children are in the acute stress response stage and tend to become sensitive and anxious. If there is no reasonable way to deal with their feelings, they may gradually develop serious emotional problems. Appropriate interventions would be necessary to prevent worse outcomes of social functioning impairment for these children. Sexual orientation is still a sensitive topic in Chinese families. Traditional Chinese families often found it hard to accept their children's sudden gender change, especially in the son-preference families. In addition, DSD may bring many challenges in terms of changes in family parenting style, education policies, and parent-child relationship, leading to difficulties in psycho-social aspects of children and their families beyond the disorder itself. In China, there are few studies on this topic. Therefore, the present study aims to evaluate the mental health status of children with DSD, and to explore the potential relevant factors.

Methods

This is a cross-sectional and case-control investigation. The recruited participants were children and adolescents aged 3-17 years diagnosed with DSD in the joint clinic from June 2019 to June 2021. The diagnostic criteria for DSD were the consensus of Chinese experts (2, 3). The criteria included that the shape of external genitalia is blurred, and two sets of reproductive systems are revealed by the B-scan ultrasonography or endoscopic exploration, or the chromosomes are not consistent with the social sex. The common feature of all DSDs was that both male and female choices were available for sex determination. The participants and their parents were interviewed with the Hamilton Anxiety (HAMA) scale. Semi-structural interviews and observations were based on the Hamilton scale to evaluate children under the age of 8 years covering the symptoms of worrying, nervousness, phobia, sleep problems, cognitive functions, depressive feelings, physical anxiety, sensory system, cardiovascular system, respiratory and digestive system, reproduction and urinary symptoms, autonomic nervous system, and relatively comprehensive evaluation of general performance, and physiological performance during the conversation (9). Children over 8 years old completed the Screen for Child Anxiety Related Emotional Disorders (SCARED), the Depression Self-rating Scale for Children (DSRSC), and the Egna Minnen av Barndoms Uppfostran-own memories of parental rearing practices in childhood (EMBU). Typically developing children and adolescents with age and gender matching were recruited as a control group. They were excluded if they had any known serious medical disorders, such as

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depression, anxiety disorder, and other mental disorders; and their parents were without serious mental health disorders.

Measures

We collected children's gender, age, physical development, and health history, the age and educational level of the parents; the pregnancy history of the mother, and the economic status of the family using questionnaires.

The HAMA, SCARED, and DSRSC were used to evaluate the mental health status of participants. HAMA was scored independently by two trained assessors through conversation and observation. HAMA divides anxiety factors into somatic and psychological factors (9). The total HAMA score can better reflect the severity of the anxiety symptoms, with a reliability coefficient of 0.93 and validity coefficient of 0.36 (10). Children with a total score higher than 7 are defined as having anxiety; those with a total score < 7 are defined as having no anxiety symptoms.

The SCARED scale was compiled by Birmaher with 41 entries. Five of these factors are parallel with anxiety disorders in the DSM-IV. Based on the children's self-assessment, the Chinese urban permanent model was revised in 2002 (11).

The DSRSC was compiled by Birleson, with 18 entries. This scale can be completed by children, and a score higher than 15 indicated that the participating children were in a depressed state (12).

The home environment scale-Chinese version (FES-CV) scale consists of 10 component tables that evaluate 10 different family social and environmental characteristics. The scale contains 90 true-false questions and has good validity, parametric reliability, and high internal consistency confidence in the affinity, ambivalence, knowledge, and organization. The individual reliability coefficients of the scale were above 0.70. The scale is available for children who have a degree above primary education (13, 14).

The EMBU was to evaluate parenting methods through **EMBU** recollection. has 81 entries and additional entries. involving 15 parenting behaviors and four main factors: rejection, emotional warmth, protection, excessive preference (15).

Statistical analysis

Data were analyzed using SPSS 22.0. The sample size of this project was calculated by the formula of $N=\mathbb{Z}^2$

 \times $(p \times (1-p))/E^2$. Thirty was the minimum sample size for quantitative research. The normality of data was tested by Kolmogorov–Smirnov test in SPSS analysis, resulting in non-normality (p < 0.05), except for the age of 8 years or older and total scores of SCARED and DSRSC (p > 0.05). Variables with normal distribution were tested with T-test, and variables with non-normal distribution were tested with non-parametric tests. The Pearson correlation analysis was used to analyze the relationships between mental health status, age, and some of the family factors in DSD children. Multiple linear regression analysis was performed to explore the related factors associated with DSDs in children's emotional states. All tests were two tailed and a p-value of < 0.05 was considered to be statistically significant.

Ethics approval and informed consent

This study was approved by the Ethics Committee of the Children's Hospital affiliated to Zhejiang University of Medicine. All parents or guardians of the included children provided written informed consent for screening and clinical treatment.

Results

Sample characteristics of the children

Thirty children with DSDs were recruited in the study. The control group included 30 typical developing children from a kindergarten, a primary school, and a middle school in Hangzhou. The average age of children in the DSD and control groups was 10.36 ± 3.50 years and 10.37 ± 3.47 years, respectively. Both groups consisted of 2 boys (6.67%) and 28 girls (93.33%). The average age of children older than 8 years old in the two groups (22 children with 21 women and a male) was 12.08 ± 2.22 years and 12.09 ± 2.16 years, respectively.

In the DSD group, nineteen of them had confirmed SRY mutations, 5 had SRD5A2 mutations, 2 had CYP17A1 mutations, and 11 had not completed relevant genetic tests. One female chromosome was (46, XX, SRY gene: negative) and one female chromosome was (46, XY [40] / 45, X (13)). Only 2 of the remaining 28 individuals (46, XY) were male.

The total HAMA score for all children in the DSD group indicated their level of anxiety was 8.10 \pm 5.57, while for the control group it was 1.50 \pm 1.55. Fifteen children (50%) in the DSDs group had a total HAMA score higher than 6, which suggested possible anxiety symptoms. However, no one in the control group reached a total HAMA score of 7. The total scores of SCARED and DSRSC for DSD group were 20.64 \pm 12.76 and 9.32 \pm 6.27, respectively. For the control group, the total scores of SCARED and DSRSC were 6.95 \pm 3.63 and 2.91 \pm 2.16, respectively.

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TABLE 1 Comparison of the he results of HAMA, SCARED, and DSRSC between DSDs children and controls.

Characteristic	Children with DSD	The control group	Statistic	P-value	
All children	n = 30	n = 30			
Age	10.36 ± 3.50	10.37 ± 3.47	Z = -0.158	0.875	
Gender					
Boy	2	2			
Girl	28	28			
Total score of HAMA	8.10 ± 5.57	1.50 ± 1.55	Z = -4.645	< 0.001	
Somatic anxiety	2.17 ± 2.34	0.57 ± 0.63	Z = -3.327	0.001	
Psychic anxiety	5.97 ± 3.96	0.87 ± 1.04	Z = -4.631	< 0.001	
Children over 8 years old	n = 22	n = 22			
Age	12.08 ± 2.22	12.09 ± 2.16	t = -0.143	0.887	
SCARED	20.64 ± 12.76	6.95 ± 3.63	t = 4.589	< 0.001	
Somatization/phobia	4.95 ± 3.51	1.68 ± 1.46	Z = 3.089	0.002	
Generalized anxiety	5.45 ± 4.84	1.14 ± 0.77	Z = -3.424	0.001	
Separative anxiety	4.45 ± 3.39	1.41 ± 1.40	Z = -3.012	0.003	
Social phobia	4.41 ± 3.03	2.32 ± 2.40	Z = -2.080	0.038	
School phobia	1.32 ± 1.25	0.41 ± 0.67	Z = -2.632	0.008	
Total score of DSRSC	9.32 ± 6.27	2.91 ± 2.16	t = 4.466	< 0.001	

Comparison of depression and anxiety disorder between DSD children and control children

Children in the DSD group had significantly higher somatic anxiety, psychic anxiety, and total anxiety scores than the control group (p < 0.001). Children with DSD had higher scores for subscales of somatization/phobia, generalized anxiety, separation anxiety, social phobia, school phobia, and higher total scores of anxiety and depression than the control group (p < 0.05 and p < 0.001, respectively). In addition, DSD children had more severe psychological anxiety than somatic anxiety. The children with DSDs had more pronounced anxiety and depression than children without DSDs (Table 1).

Relationship between anxiety, depression, age, and the FES-CV in children with DSDs

In children with DSDs, age and family entertainment in FES-CV were positively correlated with generalized anxiety score in SCARED (r=0.44, p<0.05 and r=0.34, p<0.05, respectively). Family success was negatively correlated with social phobia score (r=-0.37, P<0.05). Family contradiction was positively associated with both school phobia score in SCARED, and total DSRSC score (r=0.37, p<0.05 and r=0.36, p<0.05, respectively). No significant correlations

were found among the remaining variables. Those results suggested that the DSD children's emotions were associated with some family environmental factors (entertainment, success, contradiction) and age (P < 0.05) (Table 2).

Regression analysis of total anxiety and depression in DSD children

The total scores of depression and anxiety in DSD children were divided into factor variables. Age and family environment (entertainment, success, and contradiction) were selected as independent variables. Linear regression analysis showed that age was a major factor that affected generalized anxiety in DSD children (Table 3). The effect of age on the generalized anxiety score of SCARED was found to be statistically significant ($B=0.963,\ p<0.05$). For total scores of HAMA, SCARED,DSRSC, and subscale score of SCARED, no significant results were found for any other variables (p>0.05).

Discussion

Main findings

Children with DSD whose total HAMA score was higher than 7 points might have anxiety problems. The problem of psychological anxiety in the children with DSDs was more serious than somatic anxiety in our findings, suggesting that children with DSDs were more likely to suffer from anxiety

TABLE 2 Correlation analysis of anxiety and depression, age and the FES-CV in children with DSD.

	Somatization /phobia (n = 22)	Generalized anxiety $(n = 22)$	Separative anxiety $(n = 22)$	Social phobia $(n = 22)$	School phobia $(n = 22)$	Total score of SCARED $(n = 22)$	Total score of DSRSC $(n = 22)$	Total score of HAMA $(n = 30)$
Age	-0.2 (0.46)	0.44 (0.02)*	-0.30 (0.08)	0.17 (0.22)	0.20 (0.19)	0.13 (0.28)	0.26 (0.12)	0.36 (0.05)
Intimacy	-0.09 (0.34)	0.08 (0.36)	-0.08 (0.37)	0.04 (0.44)	-0.09 (0.35)	-0.01 (0.48)	-0.06 (0.89)	-0.23 (0.22)
Emotional	0.06 (0.40)	0.03 (0.45)	0.08 (0.36)	0.08 (0.36)	-0.07 (0.37)	0.07 (0.39)	0.07 (0.38)	0.09 (0.64)
Expression								
Conflicts	-0.07 (0.38)	0.19 (0.20)	0.15 (0.26)	-0.12 (0.30)	0.37 (0.05)*	0.10 (0.34)	0.36 (0.05)*	0.06 (0.76)
Independence	-0.16 (0.24)	-0.05 (0.40)	0.01 (0.48)	-0.17 (0.22)	0.00 (0.49)	-0.10 (0.38)	0.08 (0.36)	-0.36 (0.05)
Success	0.01 (0.47)	-0.32 (0.70)	-0.00 (0.49)	-0.37 (0.04)*	-0.18 (0.22)	-0.23 (0.15)	-0.11 (0.32)	0.16 (0.40)
Intellectual	-0.19 (0.20)	0.04 (0.44)	-0.14 (0.27)	-0.19 (0.20)	0.04 (0.43)	-0.12 (0.29)	-0.18 (0.21)	0.04 (0.84)
Entertaining	0.23 (0.15)	0.37 (0.05)*	0.13 (0.29)	0.33 (0.07)	0.07 (0.37)	0.32 (0.07)	0.26 (0.12)	0.18 (0.35)
Moral and	-0.10 (0.33)	-0.13 (0.28)	0.23 (0.15)	-0.28 (0.11)	0.12 (0.30)	-0.08 (0.36)	0.09 (0.35)	-0.00 (0.99)
Religious								
views								
Organizational	-0.22 (0.16)	0.02 (0.46)	0.01 (0.49)	0.06 (0.39)	0.14 (0.27)	-0.02 (0.46)	-0.11 (0.32)	-0.19 (0.32)
Controlling	-0.18 (0.21)	-0.21 (0.18)	-0.04 (0.43)	-0.32 (0.07)	-0.03 (0.45)	-0.22 (0.16)	-0.10 (0.32)	0.36 (0.05)

Data were presented as r (p). *P < 0.05. The bold values meant that the difference between the two factors was significant.

TABLE 3 Regression analysis of factors related to anxiety and depression in DSDs children.

	Variable	В	Standard error	Beta	T	P-value
Generalized anxiety	Constant	-6.186	5.358		-1.155	0.262
	Age	0.963	0.436	0.443	2.207	0.039
Total score of the HAMA	Constant	-0.517	4.589		-0.113	0.911
Separative anxiety	Constant	-1.851	2.851		-0.649	0.524

and depression than children without DSDs. Children with DSDs had obvious anxiety-related emotional problems, and it was associated with family environment factors (entertainment, success, and contradiction) and age. Therefore, age in children with DSDs can help with the early detection of emotional disorders and anxiety-related emotional disorders.

Importance

The findings of this study highlighted the fact that children with DSDs have relatively worse mental health status in terms of emotional conditions, such as anxiety and depressive symptoms. It confirmed the high prevalence of anxiety and depression in children with DSDs, which has been previously reported in various populations in many previous empirical studies (16). Our findings that children with DSDs had higher scores for anxiety were consistent with the findings from Johansen et al. (17, 18). Also, our findings regarding the increase in both scores of anxiety and depression were in line with results obtained from the adult group (4, 8). For children, our findings indicated a

logical link with previous outcomes that children with DSDs had significantly higher total problems reported by their parents (4). However, our findings on depression scores' increase were not consistent with the previous study by Liao et al. (18). And the main findings in the present study contradicted some results from teenagers' self-report scales showing no increase in psychological distress (4, 5, 19). These contradictions suggested the complexity of the mental health status of DSD individuals and might be due to bias that appeared during selection or from the measurements.

Infants born with DSD may undergo long-term medical and surgical management, and some patients with certain forms of DSD and gender designation had life-threatening issues and/or might have increased cancer risk (20–22). Uncertainty about illness and family environment may be important factors related to anxiety and depression in DSD children and their parents. Earlier studies have reported that higher levels of illness uncertainty were related to later decisions that parents made for their child with DSD (23). Independence, entertainment, and emotional expression were less advocated for in Chinese family environments,

with excessive emphasis on success (14). Chinese parents attached special importance to their children's success, so success is not only conducive to personal growth but also to family stability (14). Children with DSDs have a significantly different appearance of the external genital device than children without DSDs, so their family members often have severe anxiety. Perez Megan (24) conducted population surveys on mothers (n = 76) and fathers (n = 63) of DSD children, and evaluated anxiety and depression in children by self-assessment scales, quality of life scales, post-traumatic stress symptom scales, and measurements of appearance satisfaction with the child's genitalia. Lower-income, increased medical expenses, and lack of other children can increase children's psychological distress. The interaction of multiple factors, such as parenting methods, family environment, and school trauma experience, has jointly led to the occurrence, maintenance, and transformation of children's emotional disorders (24, 25).

Children with DSD needed multiple surgeries in the completion of sex distribution and subsequent treatment, which caused great psychological trauma to them. Therefore, long-term psychological evaluation and intervention are needed in these DSD children (26). In addition, children with DSD have an impaired quality of life, but this is not supported by any data (27, 28).

The study's sample size (n = 30) appeared relatively small in comparison to prior research. Through MDTrelated consultation, the coordination degree is insufficient, increasing the difficulty of enrolled patients. The sample size of this project, therefore, depended on the degree of active participation of these patients. Parents and children gave informed consent through the MDT consultation to complete the assessment content. Domestic newborn screening would detect the vast majority of DSD children in infants, and young children had begun surgical intervention. There were few children who were informed and diagnosed in other age groups. This study was a discussion of anxious mood and its related factors in this particular group. This showed that these special experiences increased the degree of anxiety in children. Awareness of early intervention and related treatment from parents should be raised in the future to lead better outcomes and quality of life for DSD children.

Concerning the age at which a diagnosis is made, the results are conflicting. Some authors suggest that age was not a linear correlation factor in the evolution of psychological distress. Rather, they supported the idea that conditions were silenced or increased by other variables that were more or less actualized depending on life stages (and related to intimate relationships, sexuality, or fertility) (16, 29). In European countries, the age at which the diagnosis was made in real life was correlated to the nature of the etiology itself. Those with late-stage diagnosis

and better outcomes were specifically asymptomatic before adolescence and could not be diagnosed earlier (16, 29). With the eugenics policy in China, parents and doctors were already preparing for intervention during their children's fetal life. There were very few children who were informed and diagnosed in childhood.

Limitations

In this study, patients aged 3-17 years with DSD from one hospital in Hangzhou were recruited. So the Berkson's bias here can hardly be avoided. A relatively high proportion of potential participants who screened positive for emotional disorder on a parental screening form refused to participate. Thus, it is uncertain whether this sample is representative of all children with DSDs in China. The diagnostic assessment of DSD children was quite rigorous, but the evaluation of family environment, parenting mode, depression, and anxiety was assessed by self-report measures. They were susceptible to a variety of biases, for example, recall bias, that was difficult to control in the analysis. In addition, the small sample size and a great majority of women in the participants may weaken the sample representativeness and the power of the study findings to some extent. In addition, the depression and anxiety measures for children (DSRSC, SCARED, and HAMA) assessed children's current symptoms at the time of the survey, which did not reflect their long-term or average level of anxiety and depressive symptoms. Lastly, long-term follow-up studies in the future are needed to clarify the interaction between the mental health status of children with DSD and its associated factors, and to describe the different clinical trajectories of children with DSD.

Conclusion

This study aims to evaluate the mental status of children with DSD, being valued by parents and professionals. Children with DSD have obvious anxiety problems, which are associated with family environmental factors (entertainment, success, and conflicts) and age. This study expands the profile of children with DSD from the psychological point, and provides the data for their psychological evaluation and intervention for them.

Abbreviations

DSD, disorders of sexual development; HAMA, Hamilton Anxiety; SCARED, Screen for Child Anxiety Related Emotional Disorders; DSRSC, Depression Self-rating Scale for Children; EMBU, Egna Minnen av Barndoms Uppfostran-own memories of parental rearing practices in childhood; FES-CV, the Home Environment Scale-Chinese version.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethics Committee of the Children's Hospital of Zhejiang University School of Medicine. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

JC and RY designed the protocol and supervised the conduct of the study. JC, WG, and GZ performed the statistical analysis. JC, HT, JY, HG, LS, and DW wrote the first draft of the manuscript. RY, GD, WR, DT, and JF provided valuable advice on the protocol and revised the draft manuscript. All authors approved the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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EDITED BY

Lawrence T. Lam, University of Technology Sydney, Australia

REVIEWED BY

Chao Xu,

The University of Oklahoma Health Sciences Center, United States Gaia Sampogna, University of Campania "L. Vanvitelli", Italy

*CORRESPONDENCE

Ioulia Kokka kokka.ioulia@gmail.com; iouliakok@med.uoa.gr

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Exploring the adult sexual wellbeing and behavior during the COVID-19 pandemic. A systematic review and meta-analysis

Iraklis Mourikis¹, Ioulia Kokka^{1*}, Elli Koumantarou-Malisiova¹, Konstantinos Kontoangelos², George Konstantakopoulos^{2,3} and Charalabos Papageorgiou^{1,4}

¹First Department of Psychiatry, National and Kapodistrian University of Athens Medical School, Outpatient Specialty Clinic for Sexual Health Eginition Hospital, Athens, Greece, ²First Department of Psychiatry, National and Kapodistrian University of Athens Medical School, Eginition Hospital, Athens, Greece, ³Research Department of Clinical, Educational and Health Psychology, University College London, London, United Kingdom, ⁴Neurosciences and Precision Medicine Research Institute "Costas Stefanis" (UMHRI), University Mental Health, Athens, Greece

Implemented social distancing measures may have forestalled the spread of COVID-19, yet they suppressed the natural human need for contact. The aim of this systematic review was to explore the impact of the COVID-19 pandemic on adult sexual wellbeing and sexual behavior. An extensive search in Pubmed, Scopus, and PsycInfo databases based on PRISMA guidelines was conducted. After applying specific eligibility criteria, screening resulted in 38 studies. Results were drawn from 31,911 subjects and outlined the negative effect of the pandemic in sexual frequency, function, satisfaction, and the behavioral changes regarding masturbation and internet-based practices. Meta-analyses of the drawn data on 1,343 female, and 1,372 male subjects quantified the degree of sexual function change during the COVID-19 pandemic vs. prior the pandemic. A random effects model revealed the significant negative impact of the pandemic on female sexual function (SMD: 0.76, 95% CI:0.74 to 1.59), while no significant change was found for the males (SMD: 0.25, 95% CI: -0.03 to 0.52). Significant heterogeneity was identified across included studies (p < 0.00001, $I^2 = 97\%$, $I^2 = 90\%$ for females and males, respectively). As part of the global health, sexual wellbeing should be on the focus of clinicians and researchers.

KEYWORDS

 ${\tt COVID-19}\ restrictions,\ sexual\ satisfaction,\ sexual\ function,\ sexual\ frequency,\ sexual\ behavior,\ pandemic\ outcomes$

Introduction

In response to the exponential growth in the COVID-19 infections' number, nations worldwide implemented lockdowns and extensive -strict or more lose- measures, which had short- and long-term effects on health systems, education, economy, and several other societal segments (1–4). The restrictions were implemented with a solid purpose to mitigate the spread of the virus, yet they suppressed the natural human need for contact, and seem to have taken a toll on people's mental wellbeing. Scientific evidence so far suggest that social distancing during the pandemic has led to higher levels of stress, and agitation (5). Leveraging data from studies in the midst of the restrictions around the globe reported elevated irritability and mood swings (6), and increases in both depressive and anxiety disorders (7), findings supported by meta-analytic reports (8).

The pandemic of COVID-19 could be perceived as a new type of trauma. Even though it does not fall into any of the Post Traumatic Stress Disorder (PTSD) models, the global scale of this stressor and the likelihood of this virus to become life threatening may result in similar symptomatology (9). For example, a large cross-national study highlighted that individuals who were infected or were afraid of getting infected demonstrated PTSD-like symptoms, introducing a "pathogenetic event memory model of traumatic stress" (10). Research has outlined that mental and sexual health undoubtfully share a strong, bidirectional link (9, 10). A large number of psychiatric anxiety-related entities demonstrate symptomatology which affect sexual wellbeing. The adverse relationship of anxiety and sexual gratification has been well documented (11, 12), as these indicators are inextricably linked to sexual desire, arousal, and satisfaction (13). Under chronic stressful circumstances, even though both males and females demonstrate increased sexual desire probably as a means of psychological relief, stressors prevent the progression of desire to actual sexual intercourse (14), resulting in reduced sexually physical contacts (15, 16). Complementary, international health associations such as WHO and CDC have highlighted the positive impact of sexual wellbeing on mental health. A healthy sexual life may function as a protective factor against psychopathology (17), while frequent sexual activity acts as a safeguard toward psychological wellness (18).

In the context of psychologically burdening feelings during the pandemic, physical intimacy -which could be considered as one of the core expressions of connection between romantic partners- could not have stayed intact, and alterations on people's sexual relationships during the pandemic were expected. Nevertheless, given the fact that each sexual act is a multi-sensory experience that can take multiple forms, body contact is not always mandatory. Thereby, the question whether the COVID-19 pandemic has affected or altered the sexual wellbeing and behavior of individuals arises.

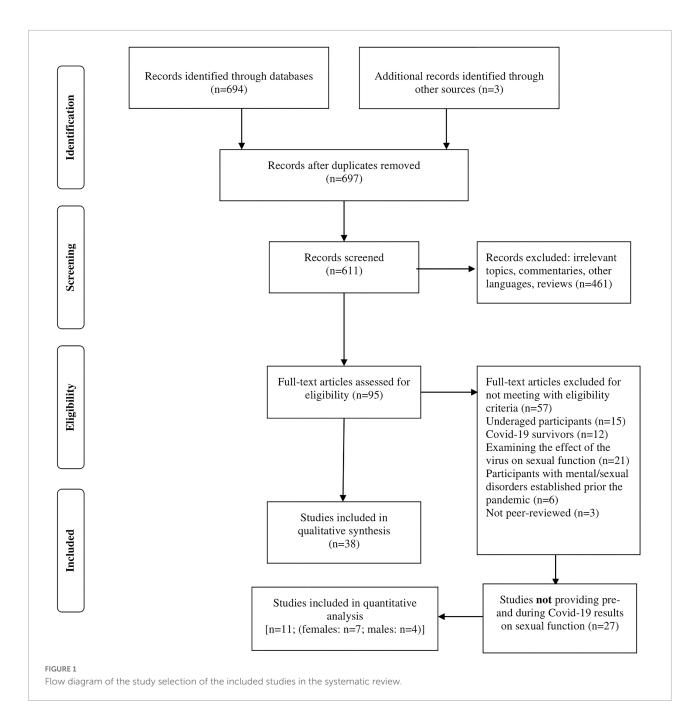
Researchers from various countries have tried to shed light on the impact of the pandemic on sexual health, and preliminary results have shown its influence on various aspects of sexual wellbeing (18, 19). However, drawing a clear conclusion based on the studies of the field could be misleading due to the diversity of the recruited samples. A few efforts to systematically approach findings on the matter have been attempted. To the authors' knowledge, these were limited and relevant to safe sexual practices regarding transmission of the virus (20), sexual minorities (21), addressed only female subjects (22), or evaluated solely sexual function (23). Thus, the primary aim of this review was to systematically explore the potential impact of COVID-19 pandemic on aspects of sexual wellbeing, quantify the change with respect to sexual function, and identify probable behavioral changes.

Materials and methods

The study was designed according the PRISMA statement guidelines (24), in order to identify papers relevant to sexual wellbeing and sexual behavior during the pandemic. Stages of research incorporated problem formulation, thorough search of the existing research in the field, data extraction and evaluation, and finally data analysis and presentation. Studies included in this review followed specific inclusion/exclusion criteria as indicated below. Sexual wellbeing is a broad construct, which lacks a sharp definition, expanding from sexual self-esteem to sexual experiences (25). For the purpose of this study, wellbeing is conceptualized as including pillars of sexual intimacy such as frequency, desire, function, and satisfaction.

Eligibility criteria

For a study to be eligible, it had to evaluate relevant to sexual wellbeing aspects (e.g., sexual function/dysfunction, activity, satisfaction etc.) and/or sexual behaviors. The study had to involve adult-only subjects, regardless of gender, age, sexual orientation, and relationship/marital status. Study groups had to derive from the general population but not on subjects with sexual dysfunction established prior the pandemic. The studies had to be published in the English language by peer-reviewed journals. Studies including females during pregnancy or postpartum were excluded, as these states have been proven to affect sexual function in a negative fashion (26, 27). Studies that included subjects with mental illnesses were excluded, because of the effect specific psychotropic medication can have on sexual function (28). Studies that investigated the biological impact of the virus on sexual function of COVID-19 survivors were also excluded. Research protocols without providing sufficient data were not included as well.



Search strategy

xPubmed, Scopus, and PsycInfo databases were thoroughly searched for relevant studies from the 1st until the 28th of March 2022. Research was conducted by two reviewing investigators, using the following terms: "sexual function" OR "sexual dysfunction" OR "sexual activity" OR "sexual health" OR "sexual satisfaction" and "sexual behavior" OR "sexual practices" OR "sexual habits" AND "COVID-19" OR "coronavirus 2019" OR "lockdown" OR "pandemic" OR "quarantine" and were adopted accordingly when necessary. Titles, keywords, and

abstracts of each study were screened for eligibility. A backward search (hand search of reference lists) of included papers was conducted to identify additional studies relevant to the topic. All yielded studies were assessed according to the eligibility criteria.

Data extraction and quality evaluation

Data extraction included country of origin, time point of the pandemic during which the study was held, the sample size

of each study, participants' mean age and gender, the aspect of sexual wellbeing under investigation, the measurements used, the main outcomes of individual studies, and any other piece of information required for the quality evaluation. The AXIS Appraisal Tool was used to assess each study's quality (29). AXIS consists of 20 items with each measuring a different aspect of a study's quality. The aim of the tool is to assist systematic interpretation of observational studies. Each question of the tool can be answered with "yes," "no" or "do not know," yet it is not used to generate a total quality score, due to the well-known problems associated with such scores (30). The procedure of data extraction was held by two reviewers. The quality of evidence was assessed with the use of the Grade of Recommendation, Assessment, Development, and Evaluation criteria (GRADE) (31). The criteria that were assessed for each study was sampling issues, consistency of methods and findings and precision of data curation.

Quantitative synthesis and meta-analysis

A quantitative synthesis of findings regarding sexual function was performed for the studies that provided adequate information. The difference between established indices of sexual function (e.g., International Index of Erectile Function, Female Sexual Function Index etc.) before and during the pandemic was calculated using the standardized mean difference (SMD) with a 95% confidence interval (CI). The Z-test was used to determine the significance of the pooled SMD. The tau² statistic was used to examine the standard deviation of underlying effects across studies. A random-effect model was applied after calculating Cochran's Q-statistic (p < 0.05) and I^2 test. A visual examination of the funnel plots was performed to estimate the publication bias. The statistical significance level was set at 5% (p < 0.05). Statistical analysis was performed using the Review Manager software (Version 5.4, the Nordic Cochrane Centre, Copenhagen, Denmark).

Results

Flow of the included studies

The initial search yielded 694 studies. After removing duplicates, and 611 titles and abstracts were screened, 95 articles were fully assessed. 57 of them were excluded for not meeting with the eligibility criteria. The final step of research resulted in 38 studies. Detailed screening procedure is illustrated in Figure 1.

Main characteristics of the included studies

All studies were observational, and more specifically of cross-sectional design. The majority was conducted in Europe (n = 23) and during the first semester of the pandemic (n = 33), with 31,911 recruited subjects in total. Mean age of the participants was 34.5 years for 32 of the studies; six of them provided only the lower age limit for participation (>18 years old). Mean percentage of female participants was 64.6% among 20 studies. Nine of them examined solely female populations, six of them solely males, while one study did not clarify participants' gender distribution. Five of the studies included exclusively coupled (married/cohabiting/non-cohabiting) participants. Four and six studies included exclusively homosexual and heterosexual participants, respectively. Five of the studies included participants differentiating their gender identity from the dyadic system (woman/man). Apart from the instruments and questionnaires used to evaluate sexual wellbeing, almost half of the included studies used tools to assess the mental state or wellbeing of their participants (n = 18). Thirteen studies used a combination of weighted questionnaires and structured interviews, 13 used solely weighted questionnaires, and 12 solely structured inquiries. Main characteristics of included studies are outlined in Table 1. Among the included studies frequency of sexual intercourse, general sexual satisfaction, sexual function, and specific sexual behaviors were examined.

Main findings regarding the research questions

Frequency of sexual activity

The domain of sexual frequency was examined by a large portion of the included studies (n = 21). Participants were asked to report their sexual frequency on a weekly basis compared to the period prior the pandemic. In the majority of the studies sexual frequency referred exclusively to partnered sexual practices (mutual masturbation, vaginal/anal penetration etc.), while in one study masturbatory or other solo activities were examined. Eleven of them found a statistically significant decrease in the number of sexual interactions during the pandemic (32-42). Notably, one study reported that about 60% of their participants did not engage in any form of partnered sexual intercourse since the outbreak of COVID-19 (39). Six of the included studies reported a decrease in the frequency of sexual activity (39, 43-48), and the proportions of participants reporting decrease ranged from 14 to 53%. However, the reduction in these studies was not statistically significant. For two of the studies no change was found (49, 50), while one, which examined the frequency of both partnered and solo practices (e.g., masturbation), reported increased frequency of sexual activity (51). Only one study found statistically significant

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TABLE 1 Characteristics of the studies included in this systematic review.

Authors, country, year of publication	Time points of study conduction	Sample's characteristics [size;gender; relationship status; sexual orientation]	Sample's age (mean age/SD, where applicable)	Aspect of sexual wellbeing/ behavior under investigation	Instruments for outcomes of interest	Main results
Cocci et al., (60) Italy	February – April 2020	n = 1515; N/A	21.0/NA	Sexual well-being during COVID-19	Questions on sexual habits pre- and post quarantine, BDI-II, BAI	Significant decrease of sexual satisfaction, >50% reported complete absence of sexual satisfaction, lower age and higher BDI scores were significant predictors of sexual dissatisfaction for both genders. Almost 40% reported increase in masturbation
Fuchs et al., (45) Poland	March-April 2020	n = 764; 100% females; 68% non-cohabiting relationship, 24.8% married, 7.2% single; N/A	25.1 ± 4.3	Female sexual function and anxiety/stress related to COVID-19	FSFI, structured questionnaire on stress and anxiety	Statistically significant decrease in all subscales of the instrument ($p < 0.001$), decrease of sexual intercourse number, increased stress and anxiety levels.
Yuksel and Ozgor, (42) Turkey	March-April 2020	n = 58; 100% females; N/A	27.6 ± 4.4	Female sexual behavior during COVID-19	FSFI, menstrual status, frequency of sexual intercourse	Significantly increased sexual intercourse, better FSFI total score, and three domain scores for arousal, orgasm, and satisfaction were significantly higher prior to the pandemic.
Cito et al., (34) Italy	April-May 2020	n=1576; 64.6% females; 35.4% males; 96.8% in a steady relationship; N/A	38.0/NA	Couples' sexuality changes during COVID-19 quarantine	Adapted scale on well-being, questions on sexual health domains and intercourse and autoerotism	Significant decline in well-being, correlation of well-being with Sexual Intercourse (SI), decreased SI, relation between reduced salary and SI, reasons for reduced SI was poor privacy and lack of psychological stimuli.
Lehmiller et al., (39) United States	March-April 2020	$\begin{split} n = &1559; 71.1\% \text{ females;} 23.4\% \text{ males } 4.5\% \\ \text{non-binary;} 52.7\% \text{ heterosexuals;} 7\% \\ \text{homosexuals;} 20.8\% \\ \text{pansexual/bisexual/other identities} \end{split}$	>18.0/NA	Changes in Sexual Behavior during the COVID-19	4-item PSS, UCLA loneliness scale-Revised, FSFI, questions on sexual changes during the pandemic, 49-item checklist on new sexual behaviors	43.5% reported a decline in the sexual life. Decreased sexual behaviors, 20.3% reported a new addition of sexual behaviors from the provided checklist.
Schiavi et al., (40) Italy	February-March 2020	n = 89; 100% females; N/A	39.0/NA	Female sexual function during lockdown	FSFI, FSDS, SF-36	Participants reported significant decrease in FSFI, and significant increase of FSDS scores post quarantine.
Arafat et al., (49) Bangladesh, India, Nepal	April 2020	n = 120; 77.5% males; 21.7% males; 0.8% unidentified; 100% married	35.42 ± 5.73	Sexual behavior of married couples during lockdown	structured questionnaire on sexual life	45% of the respondents reported that lockdown had some effect on their sexual intercourse number. 50% reported a positive effect on their emotional bonding with their spouse
Ilgen et al., (53) Turkey,	January-February 2020	$n=52; 100\% \ females; 100\% stable$ $relationship; 100\% heterosexual$	35.1 ± 5.8	Female sexual function during COVID-19 pandemic	FSFI, BDI, BAI	FSFI scores of the participants were higher before the pandemic, however, this finding was not statistically significant. BAI scores had a negative correlation with FSFI scores.
Bhambhvani et al., (50) United States,	March 2020	n=91;100% females; 82.4% stable relationship; 15.4% single; N/A	43.1 ± 11.8	Impact of the COVID-19 pandemic on female sexual function and frequency	FSFI, PHQ-4	Statistically significant decrease in FSFI total scores pre- and during- the pandemic. No significant change in sexual frequency was reported by most of the participants.
Sotiropoulou et al., (54) Greece,	April-May 2020	n = 299; 71.2% females; 29.8% males; 100% stable relationship;100% heterosexual	43.2/NA	Sexual function and relationship quality of heterosexual couples during the quarantine	FSFI, IIEF, structured questionnaire on sexual activity, relationship quality, and mood and anxiety	No statistically significant difference of FSFI scores pre- and during the pandemic. IIEF was statistically higher during the pandemic. Weak associations between depressive mood and anxiety and sexual well-being were reported.

(Continued)

TABLE 1 Continued

Authors, country, year of publication	Time points of study conduction	Sample's characteristics [size;gender; relationship status; sexual orientation]	Sample's age (mean age/SD, where applicable)	Aspect of sexual wellbeing/behavior under investigation	Instruments for outcomes of interest	Main results
Karagoz et al., (55) Turkey,	May 2020	n=245;39.6% females;100% stable relationship; 100% heterosexual	35.9 ± 6.9	The effect of COVID-19 pandemic on couples' sexuality	GAD-7, PHQ-9, PSS, FSFI, IIEF	Thoughts for contraction during sexual intercourse were expressed ($p = 0.002$). Increased masturbation ($p = 0.022$). Significant decrease in the erectile and orgasmic function, intercourse satisfaction, and overall satisfaction scores ($p = 0.001$, $p = 0.014$, $p = 0.001$, respectively). Statistically significant decrease in lubrication, orgasm, and satisfaction in women ($p = 0.034$, $p = 0.023$, $p = 0.007$).
Carvalho et al., (56) Portugal,	March-June 2020	n=662;62.9% females; 37.1% males;100% heterosexual; 61.6% cohabiting partners; 38.4% single	38.0 ± 12.0	Examination of the relationship between COVID-19 confinement and sexual functioning domains in heterosexual males and females	Self-reported levels of confinement and psychological adjustment during lockdown, IIEF, FSFI	Psychological adjustment mediated the effects of confinement in male sexual desire, erectile function, sexual satisfaction, and overall satisfaction; no mediating effects were found regarding orgasmic function. No significant correlation of confinement and female sexual function. Increased psychopathological symptomatology predicted lower levels of sexual desire, lubrication, arousal, satisfaction, and orgasm.
Karsiyakali et al., (37) Turkey,	June 2020	n = 1356; 50.5% females;49% males; N/A 47.8% married; 52.2% single; N/A	33.1 ± 8.31	The effects of the COVID-19 pandemic on the sexual functioning	IIEF, FSFI, questionnaire on sexual desire, masturbation and number of intercourses	Statistically significant decrease in sexual desire, masturbation and number of sexual intercourses. Being single, not having a child, having a regular sexual partner, and being unemployed were associated with a decline in sexual intercourse frequency and sexual desire.
Wignall et al., (58) United Kingdom,	May 2020	n = 467; 59.8% females; 60.4% stable relationship; 32.6% single; 7% causal relationship;86% heterosexual; 14% homosexual	25.3 ± 4.13	Changes in Sexual Desire and Behaviors during lockdown	SDI-2, sexual behavior catalogue, SOI-R	Significantly decrease in sexual desire for females, insignificant decrease for males. Sexual behaviors reduced during the pandemic, 20% reported increased use of pornography. 33% reported having less sex, and 25% masturbating less. Men and LGB individuals reported greater increases in sexual activity than women and heterosexuals.
Panzeri et al., (48) Italy,	April-May 2020	n=124;73.4% females;26.6% males;94.4% heterosexual; 4% bisexual;1.6% homosexual	34.01 ± 8.71	Changes in sexuality and quality of couple relationship during the COVID-19 lockdown	BISF-W, SDI, DASS-21, PHQ-15, QMI	No changes in sexual desire, arousal, and orgasm during lockdown for males and females. 24.2% of the males and 30.8% of the females reported a decrease in sexual frequency
Luetke et al., (38) United States,	April 2020	n = 742; 51.0% females; 49% males; 81% stable relationship; 19% single; N/A	44.0/NA	Changes in intimate and sexual behaviors and experiences during COVID-19	UCLA Loneliness scale, CES-D-10, questions on sexual behaviors and frequency, and orgasm and emotional closeness	Frequent coronavirus-related conflict was significantly predictive of decreased frequency of solo and partnered intimate and sexual behaviors.
Hille et al., (36) Germany, Switzerland and Austria,	April 2020	n = 2515; 47.4% females; 53.6% males; 77.6%; N/A; heterosexual;13.2% bisexual; 6.7% homosexual; 2.4%pansexual	44.0/N/A	Changes in sexual behavior during the COVID-19 pandemic	Questionnaire on sexual activities and practices, personal satisfaction	Significant decline in frequency of sexual activities since the distancing measures. Only anal intercourse showed no significant decrease. Those in a relationship masturbated significantly less during the pandemic.

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TABLE 1 Continued

Authors, country, year of publication	Time points of study conduction	Sample's characteristics [size;gender; relationship status; sexual orientation]	Sample's age (mean age/SD, where applicable)	Aspect of sexual wellbeing/ behavior under investigation	Instruments for outcomes of interest	Main results
Baran and Aykac, (33) Turkey,	June 2020	n = 536, 100% males; 75.4% stable relationship; 24.6% single; N/A	38.6 ± 10.3	Effect of COVID-19 fear on sexual behavior	IIEF, questions on fear of transmission and changes in sexual behavior	19.4% (104) developed fear of COVID-19 transmission from the sexual partner. Statistically significant decrease of weekly sexual intercourse
Cascalheira et al., (65) United Kingdom,	May 2020	n = 565, 59.8% females; 38.9% males; 0.9% non-binary; 86.1% heterosexual; 9.2% bisexual; 4.6% homosexual	25.4 ± 4.1	Changes in Sexual Fantasy and Solitary Sexual Practice	Questions on solitary sexual behaviors, sexual fantasies and pornography consumption	34.3% engaged in more sexual fantasizing, 30.44% reported an increase in solitary sexual practice, increase in pornography use for 19%
Gouvernet and Bonierbale, (62) France,	April-May 2020	n = 1079; 68.7% females; 31.3% males; 20.7% single; 79.3% stable relationship; N/A	>18.0/NA	Impact of COVID-19 on sexual cognitions and emotions	SMQ, GAD7, MDI, ECR-RS, questions on sexual frequency and satisfaction	Decrease in sexual frequency and satisfaction, which affected mostly women, and were related to negative sexual cognitions and less positive sexual emotions. Increases in digital sex use contributed to minimizing the likelihood of negative sexual motions
Hammoud et al., (46) Australia,	April 2020	n = 940, 100% males; N/A; 92.7% homosexual; 7.3% bisexual	39.9 ± 13.4	Disrupted Sexual Behaviors Among Gay and Bisexual Men	Questions to measure changes in sexual behaviors	84.2% reduction is sexual intercourse during the pandemic compared to before the outbreak
Osur et al., (64) Kenya,	September 2020	n = 194, 39.2% females, 60.8% males; 100% married; heterosexual	>18.0/NA	Perceived and experienced sexual satisfaction among married couples during COVID-19	Questionnaire adapted from the Index of Sexual Satisfaction	41.3% reported being sexually dissatisfied, 26.6% reported being dissatisfied prior to the pandemic. Significant difference when comparing before and during COVID-19 sex satisfaction ($\chi^2 = 38.86, p < 0.001$).
Mumm et al., (52) Germany,	April-July 2020	n = 414, 100% cis males; 62.1% stable relationship; 37.9% single; N/A Hetero- Homo- and Bisexual	>18.0/NA	Sexual Behavior of Hetero-, Homo-, and Bisexual Males	Sexual Behavior Questionnaire	Average weekly frequency of sexual intercourse and masturbation was increased in all groups, significant rise satisfaction with the sexual frequency, level of sexual arousal increased significantly in all groups, joy from sexual intercourse or masturbation increased significantly in heterosexual ($P < 0.005$) and homosexual men ($P < 0.005$)
McKay et al., (67) United States,	April-May 2020	n = 728, 100% males; 53.7% stable relationship; 46.3% single; N/A homosexual, bisexual	>18.0/NA	Sexual Behavior Change Among Gay and Bisexual Men	Questions on sexual behavior	9 out of 10 participants reported having sex with a stable partner or no sex at all. Reporting no sexual partners in the last 30 days was significantly predicted by increased exposure to a Stay-at-Home order. Increased masturbation and cyber-sex. HIV-positive men were particularly likely to adopt strategies including avoiding casual partners
López-Bueno et al., (51) Spain,	March-May 2020	n=536,72.8% females; 27.2% males; 33.2% stable relationship; 66.8% single; N/A	>18.0/NA	COVID-19 Confinement and Sexual Activity in Spain	Questions on sexual activity	No significant difference in sexual activity was reported, particularly for those married or in a domestic partnership.
Gasso et al., (68) Spain,	March-June 2020	n = 293, 66.2% females; 32.8% males; 1% unspecified; 83.6% heterosexual; 5.1% homosexual; 10.2% bisexual; 41% single; 59% stable relationship	30.3 ± 13.0	The prevalence of sexting and online sexual victimization behaviors	Sexting items adapted from the Juvenile Online Victimization Questionnaire	Sexting engagement and online sexual victimization decreased during lockdown despite the increase in internet use

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TABLE 1 Continued

Authors, country, year of publication	Time points of study conduction	Sample's characteristics [size;gender; relationship status; sexual orientation]	Sample's age (mean age/SD, where applicable)	Aspect of sexual wellbeing/ behavior under investigation	Instruments for outcomes of interest	Main results
Shilo and Mor, (66) Israel,	March-April 2020	n = 2562; 100% males; 100% homosexual; 81.6% single; 18.4% stable relationship	37.0 ± 11.3	Changes in sexual behavior of MSM during the COVID-19 pandemic	questions on sexual activity, practices, frequency and number of partners	39.5% continued to meet new casual sex partners. Being younger, single, and with higher mental distress predicted engagement in casual sex. MSM reduced their sexual risk and limited sexual repertoire
Neto et al., (63) Brazil,	July-August 2020	n = 1314; 70.6% females; 29.4% males; 89.2% heterosexual; 10.8% homosexual; 82.6% steady relationship; 17.4% single	37.6 ± 10.8	Impact of the pandemic on sexual function	FSQ, MSQ, questions on sexual behaviors and libido	Worsening of sexual satisfaction was reported by 44.5% of the participants, with the following associated factors: Lower libido, missing Nightlife, Higher Masturbatory Frequency, and isolation from the partner. Worsening of Libido was reported by 37%.
Costantini et al., (59) Italy,	May 2020	n = 2149, 51.7% females; 48.3% males; 94% heterosexual; 10% bisexual; 4% homosexual; 84.2% stable relationship; 15.8% single	43.0 ± 12.5	Changes in the sexual behavior of adult men and women in stable relationships	IIEF, FSFI, marital adjustment test, Hamilton Anxiety Rating Scale	The sex lives improved for 49% of participants, particularly those in cohabitation, for 29% it deteriorated, while for 22% of participants remained stable.
Ballester-Arnal et al., (43) Spain,	April 2020	n = 1478; 67.5% females; N/A; N/A	31.92 ± 10.1	Sexual habits of the general population during lockdown	Questions on sexual desire and activity, masturbation, sexual relationships, online sexual activity, sexual fantasies and urges	Confinement affected the sexual life of almost half of the sample (47.7%), mostly females. Those with a worsen sexual life were 3 times more (37.9%) than those who reported an improvement.
Coombe et al., (44) Australia,	April-May 2020	n = 965; 70.0% females; 25.6% males; 4.4% gender diverse; 61.8% stable relationship; 38.2% single; 65.7% heterosexual; 29.4% homosexual; 4.9% bisexual	24.0/NA	Impact of lockdown on sexual practices	Questions on trends and changes in sexual practices, intimate relationships	53.5% reported less sex during lockdown. Solo sex activities increased; 14.6% reported using sex toys more often and 26.0% reported masturbating more. Using dating apps for chatting/texting and setting up virtual dates increased during lockdown.
Ates et al., (32), Turkey	November-December 2020	n=602,100% males; $60.1%$ married; $39.9%$ single; N/A	36.1 ± 11.6	Heterosexual male changes in sexual function and behavior	IIEF, IELT, PEDT, sexual intercourse frequency	Statistically significant reduction of sexual frequency ($p < 0.001$), total IIEF score significantly lower ($p < 0.001$), subscales of sexual function and satisfaction were significantly higher ($p = 0.016$, $p < 0.001$ respectively). PEDT score significantly higher ($p = 0.004$). No significant difference in IELT.
Szuster et al., (41) Poland	April-May 2020	n = 1644, 100% females; 83.1% stable relationship; 16.9 single; N/A	25.11 ± 7.09	Impact of COVID-19 on mental and sexual health of reproductive aged women	FSFI, BDI	Lower frequency of sexual activity ($p < 0.001$) and a lower libido level ($p < 0.001$). Mean FSFI total score was 27.01 \pm 7.61. SFI and BDI scores were significantly correlated ($P < 0.001$).
Gleason et al., (61) United States	October 2020	n = 1051, 57.3% males; 42.7% males; 65.5% stable relationship; 34.5% single; 88.3% heterosexual; 3.4% homosexual; 6.3% bisexual; 1.1% pansexual	38.54 ± 10.56	Impact of COVID-19 on sexual behaviors	Questions on sexual frequency, satisfaction and sexual/physical violence	Significant but small $(d < 0.2)$ increase in masturbation and pornography use for males. Significant decrease in sexual desire for females. Small significant decreases $(d > 0.2)$ sexual enjoyment/pleasure, and a medium significant decrease $(d > 0.5)$ was noted for frequency of sex with casual partners
Grover et al., (35) India	May-June 2020	n=450, 85.6% males; 14.4% females; 95.1% stable relationship; 4.8% single; N/A	41.5 ± 11.2	Sexual function during the pandemic	CSFQ, PHQ-4	Statistically significant reduction in sexual frequency ($p < 0.001$) and intimate contact when not involved in sexual practices, e.g., hugging/cuddling ($p = 0.042$).

TABLE 1 Continued

Authors, country, year of publication	Time points of study conduction	Sample's characteristics [size;gender; relationship status; sexual orientation]	Sample's age (mean age/SD, where applicable)	Aspect of sexual wellbeing/ behavior under investigation	Instruments for outcomes of interest	Main results
Caruso et al., (69) Italy	Not provided*	n = 317, 100% females; N/A; N/A	18-48	Sexual activity and contraception use during the pandemic	Structured inquiry regarding contraception and sexual activity	All married and cohabiting women were continuing to use their contraceptive method. 50.5% non-cohabiting or single women had discontinued their contraception method while social distancing, for non-method-related reasons. 46.5% non-cohabiting or single women had continued their sexual activity, infringing social distancing rules, and 14.9% had had an unplanned pregnancy, for which they had sought a termination.
Kusuma et al., (47) Indonesia	November-December 2020	n = 131, 48.9% females; 51.1% males; 71.9% married; 28.1% single; 96.1% heterosexual; 2.2% homosexual; 1.5% bisexual	28.7/N/A	Differences in mood and sexual activity during COVID-19	DISC, questions on behavior, and frequency of sexual intercourse before and during COVID-19 pandemic	53.8% of respondents admitted that the COVID-19 pandemic affected their sexual activity. No significant difference in condom use between before and after the pandemic was noted.
Chatterjee et al., (57) India	July-August 2020	N = 1376, 80.5% males; 19.4% females; 65.9% married; 34.1% single; N/A	34.42 ± 9.34	Association between sexual function and mental comorbidities and quality of life during the pandemic	DASS21, ASEX, WHOQOL-BREF	27.18% reported having a sexual dysfunction based on the ASEX instrument. Increase in age and female gender were associated with sexual dysfunction overall and also all its components. Increased depressive symptomatology was associated with lack of orgasm, and sexual satisfaction.

SD, Standard Deviation; FSFI, Female Sexual Function Index; PSS, Perceived Stress Scale; BDI-II, Beck's Depression Inventory-II; BAI, Beck's Anxiety Inventory; STAI, State-Trait Anxiety Inventory; CES-D-10, Center of Epidemiologic Studies Depression Scale, SF-36, 36 Short Form Health Survey, SF-36, 36 Short Form Health Survey, GAD-7, Generalized Anxiety Disorder-7, PHQ-9, Patient Health Questionnaire-9, ISS, Index of Sexual Satisfaction; SDI-2/SDI, Sexual desire inventory; SOI-R, Sociosexual orientation inventory-Revised; ECR-RS, Experiences in Close Partner Attachment Scale; MDI, Major Depression Inventory; SMQ, Sexual Mode Questionnaire, FSQ, Female sexual quotient; MSQ, Male sexual quotient, BISF W/M, Brief Index of Sexual Functioning (Women/Men); QMI, Quality of Marriage Index; FSDS, Female Sexual Distress Scale; MSM, males having sex with males; IELT, Intravaginal ejaculatory latency time; PEDT, Premature ejaculation diagnostic tool; CSFQ, Changes in Sexual Functioning Questionnaire; PHQ-4, Patient Health Questionnaire-4; DISC, Depression Intensity Scale Circles, DASS21, Depression Anxiety Stress Scale 21; ASEX, Arizona Sexual Experience Scale; WHOQOL-BREEF, WHO quality of life questionnaire; Authors have tried to contact the research team in order to find the time frame of the study without success.

increase in partnered sexual activity, with almost 30% being sexually active more than three times per week (52).

Sexual function

Sexual function and potential indications of sexual dysfunction were explored by 14 of the included studies. The majority of these studies (n = 12) examined this domain with the Female Sexual Function Index and the International Index of Male Function while the remaining with questionnaires structured by the researchers, and results could be considered contradicting. Eight included solely female participants, seven of which compared their results with pre-COVID data. Among them two reported statistically significant decreases in all domains of sexual function (desire, arousal, lubrication, arousal, satisfaction, and pain) (40, 45), and one came into similar decreases, yet those were statistically insignificant (53). Two of them found significant decreases for the global sexual function, but when subdomains were accessed separately, they concluded in statistical decrease only for arousal, lubrication, and satisfaction (42, 50). In two studies sexual function was evaluated for both male and female participants and no significant change was found for either of their subgroups (48, 54). In contrast, another study reported significant decreases for their female participants but only for the lubrication, orgasm, and satisfaction subdomains of sexual function, whereas significant decreases in global function and erectile and orgasmic function, and satisfaction sub-domains were found for their male participants (55). Two of the studies found that lowered sexual function was present only when the psychological burden of the restrictions was assessed as high (56), and mostly for females and older participants (57). Three of the included studies evaluated solely sexual desire. One found decrease for males and females but this was significant only for females (58), while the second one reported significant decrease for both sexes (37). Though Cito et al. reported a decreased number of sexual intercourses, they found stable and in a subset of the subjects increased levels of sexual desire (34). Ates et al found a significant reduction in IIEF total scores, but a significant increase for the subscale of sexual function, and significant increase in the premature ejaculation diagnostic tool (32).

General sexual satisfaction

General satisfaction deriving from the sexual life of individuals was examined by 15 of the included studies. One of the studies concluded in improved levels of satisfaction for more than 50% of their participants (49), while in one stability (22%) and improvement (49%) was found (59). Two of the studies found that only a small portion of their participants reported decreased sexual satisfaction and, akin to other studies, this occurred only in those demonstrating high levels of anxiety (53, 56). Five of them found a statistically significant decrease, while for one of them this was more prominent for

the female participants (34, 41, 60–62). Interestingly, in one of them 50% reported complete absence of satisfaction (60). Among four of the studies, the reported deteriorated satisfaction ranged from 41.3 to 50% (39, 43, 63, 64), while experiencing fear and anxiety for contracting the virus and increased depressive symptomatology was significantly associated with lower sexual satisfaction (33, 41). Mumm et al who included solely males, resulted in increased sexual satisfaction but only for those of hetero- and homosexual orientation, and not for bisexual men (52).

Sexual behavioral changes

Seventeen of the included studies attempted to report on possible behavioral changes with respect to sexual life, such as masturbation frequency, online activities etc. Masturbation was examined by seven studies. All found a significant increase of masturbation (39, 43, 52, 55, 61), and the percentages of this increase ranged from almost 15 (44) to 40% (60) of the participants. On the contrary, three of the studies reported the exact opposite; a decrease in masturbation was found (58), however this was significant only for participants in stable and cohabiting relationships (36, 37). Digital and internet-based sexual practices were examined by a portion of the studies (n = 6). Three of them found an increase in pornography use, and this was reported by a similar percentage of participants (≈20%) across all studies (58, 65, 66). A 33% increase in cybersex was reported by one of the studies (67), while one found that almost 30% of their participants created and shared sexual, digital content for the first time (68), and one reported an increase in dating applications use and virtual dating (44). Changes in the sexual repertoire were additionally examined. Cascalheira et al found that more than 30% of their participants expanded their solo sexual practices such as fantasizing more (65), while Lehmiller et al reported additions in their participants' sex lives, which included new positions during intercourse (1/5 of the participants), sharing (13%) and acting (8.5%) on fantasies, and using sex toys (7.3%) (39). Sexual positions were examined by one more study, which found statically significant decrease in face-to-face positions in order to avoid transmission of the virus (32). Behaviors of intimacy were similarly deteriorated, with two studies reporting significant reduction of romantic practices such as hugging or cuddling (35, 36). Two of the included studies examined the use of contraceptive measures, and results were contradicting; one revealed a more than 50% decline for non-cohabiting partners (69), and one reported no change (47). Three studies, which all included males who have sex with males, concluded in contradicting results; two found increased masturbation and cybersex (67), and avoidance of casual sexual intercourse with this reaching 15times fold reduction (46), while Shilo and Mor reported that almost half of their participants continued casual intercourse, but with limited repertoire (66). A summary of the findings are reported in Table 2.

Factors affecting sexual wellbeing and behavior

Some of the included studies tried to identify factors which mediated the relationship between sexual wellbeing and the pandemic. Factors regarding sociodemographic characteristics, as well as psychological characteristics were found to affect this relationship. The most prominent characteristic was that of gender; women appeared as mostly affected in a negative manner (43, 58, 61, 62) Socio-economic status (39), and reduced salary due to work suspension (34), unemployment (37, 59), lack of privacy (43, 48), younger age (39, 60, 66), and being single (69) were identified among these factors. With respect to psychological characteristics, increased depressive symptomatology (48, 53, 60), anxiety (48, 54), stress (32, 48), and loneliness (41) were identified to negatively affect sexual wellbeing. In addition, fear of contracting the virus was found to act as a restrictive factor of sexual wellbeing (41).

Quality assessment

Two independent reviewers assessed the quality of individual studies with the Appraisal Tool for Cross-Sectional Studies (AXIS). Each study's quality was evaluated

TABLE 2 Summary reporting on changes in main outcomes of interest.

Sexual variable	Studies (ref. no)	Change in Outcome
Frequency $(n = 21)$	(32-42)	Statistically significant decrease
	(39, 43-48)	Statistically insignificant decrease
	(49, 50)	No change
	(51)	Statistically insignificant increase
	(52)	Statistically significant increase
Satisfaction $(n = 15)$	(34, 41, 60-62)	Statistically significant decrease
	(33, 39, 43, 63, 64)	Statistically insignificant decrease
	(49, 52, 53, 56, 59)	Statistically insignificant stability/increase
Behavioral	(39, 43, 44, 52,	Statistically significant increase in
changes $(n = 17)$	55, 60, 61)	masturbation
	(36, 37, 58)	Statistically insignificant decrease in masturbation
	(44, 58, 65–68)	Statistically significant increase in internet-based sexual practices
	(32, 35, 36, 39, 47, 69)	Alteration/expansion of sexual repertoire
Function	(32, 36, 37, 40,	Statistically significant decrease
(n = 14)	42, 45, 50, 55–58)	
	(34, 48, 54)	No change
	(53)	Statistically significant increase

independently by each reviewer and juxtaposed their results; no disagreements occurred. Overall quality did not vary significantly across studies, with most of them being of moderate quality. The main quality issues were the lack of information on non-responders, and questionable internal consistency of several studies due to the use of not validated instruments. An additional quality issue regarding sampling that needs to be addressed is the fact that all of the studies recruited their samples online, questioning their representativeness. Detailed outcomes of the quality evaluation are presented in Table 3. The GRADE evaluation method uses a 4-level system of evidence grading, with randomized control trial being the only type of study design that can receive 4/4 (high level of evidence). Given that all included studies were observational, the highest possible grade was 3/4 (moderate level of evidence), unless there was a reason to upgrade or downgrade. The risk of bias was assessed by evaluating the representativeness of sampling, and the measurement and reporting bias. The vast majority of the studies downgraded to 2/4, given the unjustified samples' size (n = 35), and the use of structured inquiries to evaluate outcomes of interest (n = 15).

Quantitative synthesis and meta-analysis

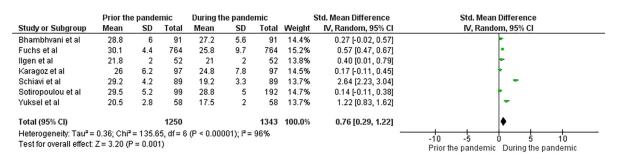
Among the included studies, only seven provided the required pre- and during-the pandemic data for their female participants, and four for their male participants. With respect to females, the random effects model revealed that the Female Sexual Function Index (FSFI) total scores showed a statistically significant difference between pre-COVID and during-COVID total scores for their participants (SMD: 0.76, 95% CI:0.74 to 1.59, z summary effect size p = 0.01) (Figure 2). Regarding males, the model showed that IIEF total scores demonstrated no significant difference between pre-COVID and during-COVID total scores for their participants (SMD: 0.25, 95% Cl: -0.03 to 0.52, z summary effect size p = 0.08) (Figure 3). A significant heterogeneity was identified across included studies (p < 0.00001, $I^2 = 97\%$, I² = 90% for females and males, respectively). Visual examination of the funnel plots indicated the risk of publication bias over included studies (Figures 4, 5). Given the high heterogeneity of the studies, the authors intended to perform a meta-regression to investigate whether the results were influenced by other covariates. Due to the lack of adequate data, this was not feasible. However, among the covariates, the severity of the pandemic among different countries, the different type of restrictions implemented, or the different relationship status among the participants could be identified.

TABLE 3 Quality assessment of individual studies included in the systematic review based on the AXIS tool.

STUDY

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ITEM	Cocci	Fuchs	Yuksel	Cito	Lehmiller	Schiavi	Arafat	Ilgen	Bhambhvani	Sotiropoulou	Karagoz	Carvalho	Karsiyakali	Wignall	Panzeri	Luetke	Hille	Baran	Cascalheira	Gouvernett	Hammond	Osur	Mumm	McKay	Lopez-Bueno	Gasso	Shilo	Neto	Costantini	Ballester -Arnal	Coombe	Ates	Szuster	Gleason	Grevor	Caruso	Kusuma	Chateerjee
Clearly stated objectives	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Appropriate study design	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Population clearly defined	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y
Representantive sample	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y
Proper selection process	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	Y
Address non-responders	N	N	N	N	N	Y	N	N	N	Y	N	N	N	N	N	N	N	Y	N	N	Y	Y	N	N	N	N	Y	N	Y	Y	Y	N	Y	Y	Y	N	N	Y
Appropriate measures	D	Y	Y	Y	Y	Y	D	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	D	D	Y
Reliable measures	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	D	Y	D	Y	D	D	D	Y	D	Y	Y	Y	Y	Y	Y	D	Y	D	D	Y
Determined stat. significance	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y
Sufficient methods description	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Data adequately described	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y
Possibility of non-response bias	Y	D	D	Y	D	N	Y	D	D	N	D	D	D	D	D	D	Y	N	D	D	D	N	D	D	D	D	N	N	N	D	N	D	N	N	N	Y	Y	N
Non-responders information	Y	N	N	N	N	Y	N	N	N	Y	N	N	N	N	N	N	N	Y	N	N	N	Y	N	N	N	N	Y	N	Y	Y	N	N	Y	Y	Y	Y	N	Y
Results internally consistent	D	D	Y	D	D	Y	D	Y	Y	D	Y	Y	Y	Y	Y	D	Y	Y	D	D	D	Y	D	D	D	Y	D	Y	Y	D	D	Y	Y	D	Y	D	D	Y
Results based on methods	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Results justify conclusions	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Limitations	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y
Conflict of interest	Y	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	D	N	N	D	D	D	N	N	N	N	Y	N	N	N	N	N	N	N	N	N	N	Y
Ethics approval	D	Y	Y	D	Y	Y	D	Y	Y	Y	Y	Y	Y	Y	Y	Y	D	Y	D	D	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

Y, Yes; N, No; D, Do not know.



EIGHDE 2

Forest plot presenting the meta-analysis based on SMDs for the effect of the pandemic on female sexual function.

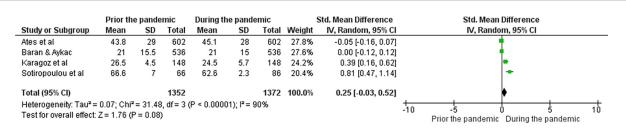
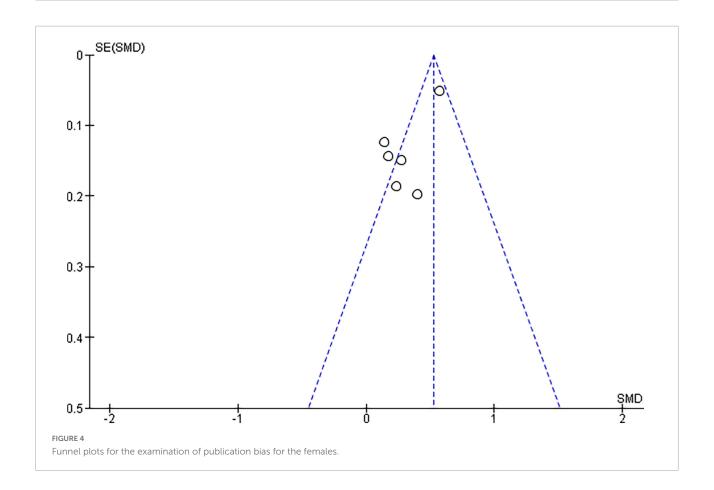
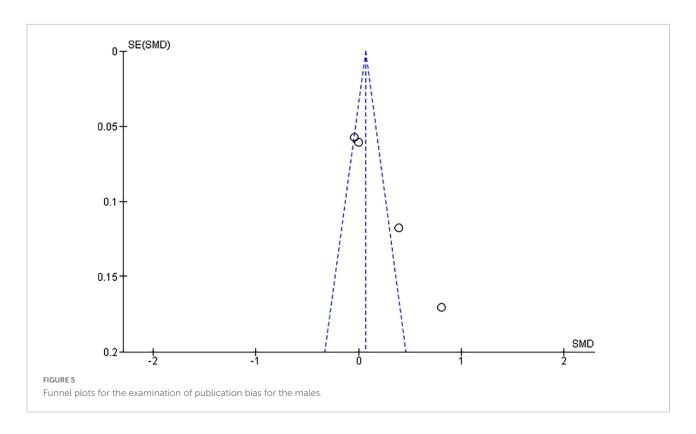


FIGURE 3

Forest plot presenting the meta-analysis based on SMDs for the effect of the pandemic on male sexual function.





Discussion

This systematic review aimed to examine the existing body of evidence regarding the influence of the COVID-19 pandemic on the sexual wellbeing and sexual behaviors of adults. Findings on the matter appeared to be rather consistent across studies, and partially supported by the meta-analytic outcomes. A deterioration of sexual wellbeing with lowered frequency of sexual activity, diminished satisfaction and, for some, problematic sexual function was found, whereas in only a small number of studies the pandemic was presented as an opportunity to reinvent intimate relationships. The relation of the participants' psychological state and sexual wellbeing was evident. Sexual wellbeing and discomforting feelings, such as anxiety, increased stress, depressive symptomatology, and perceived lower quality of life were associated in a large portion of the included studies. However, the causal relationship could not be defined with certainty. As far as changes in sexual behavior are concerned, results were rather contradicting regarding masturbation, while a rise in internet-based sexual practices, and changes in sexual repertoire were documented.

Sexual function was the only aspect of sexual wellbeing for which data could be drawn to perform a meta-analysis. Results from the quantitative synthesis revealed a statistically significant negative effect of the pandemic on female sexual function. Taking into consideration that for most of the studies lower sexual function was linked to lowered quality of life and increased anxiety levels, this came in line with previous

findings, which showed that chronic daily stressors can affect genital arousal and impair female sexual function (70). On the contrary, meta-analytic findings for the male sexual function showed no significant alteration. It may be supported that the meta-analytic findings outline the moderating role of gender, which emerged in several of this review's studies (43, 48, 56, 58, 62). This could be partly explained by the fact that males are less susceptible to chronic stress (71). Because of different levels of exposure to psychological and social pressure, and increased vulnerability due to biological factors, women are more likely to be affected by stressful circumstances compared to men (72). However, it could be argued that the meta-analytic results for the male participants are not representative of the actual case. Among the included studies, those with the largest male samples demonstrated statistically significant reductions in sexual function, even though the comparison with pre-pandemic scores was not feasible. An additional argument could be that the IIEF index perceives male sexual function in a somehow narrow manner, since it examines solely penile rigidity and penetration, without assessing other ways males can engage in and enjoy sexual intercourse. Complimentary, a plausible explanation for the statistically insignificant findings could be the reported increase of medication regarding male sexual dysfunction. A recent study found that between February and December of 2020 a 67% increase in sales of phosphodiesterase-5 inhibitors (PDE5-Is) was noted in the United States, and more particularly, an 85% increase of tadalafil sales (73). This suggests that men's

function might not have been affected, but pharmaceutical assistance was required.

With respect to sexual frequency, the limited number of intercourses could be characterized as expected. Literature has shown that emotional and physical intimacy play a crucial role in sexual desire and maintenance of sexual activity (74), while the time shared between non-cohabiting partners, is the predominant predictor of negatively affected sexual interactions (75). Taking into consideration that many of the studies were conducted during complete quarantines and included participants who did not cohabit with their partner (36, 37, 58, 65), the impact of relationship status and a decrease in the frequency of partnered sexual interaction were anticipated. Surprisingly, this decrease applied for co-habiting partners in one of the studies as well (45). Though desire for sexual intercourse was reported as insignificantly changed or even higher by some of the studies, this did not progress into actual contact. This could be explained by findings which reported that the fear of contracting the virus minimized physical contact between partners (76). In addition, other findings supported that ruminating COVID-19-related conversations reduced the couples' ability to avoid conflict, and decreased intimate expressions that could progress into sexual contact (77). The disagreement found between sexual desire and sexual intercourse, comes in accordance with what was found by Morokqff and Gillilland; males and females under the same stressful circumstances did demonstrate higher sexual desire, yet stressors prevented the progression of desire to actual sexual intercourse (78). Though sexual desire and frequency were expected to down escalate as age of participants increased (79), a portion of the studies did not verify the role of age in sexual life (37, 39, 45).

Likewise, the overall satisfaction deriving from sexual life was mostly affected in a negative fashion. Results showed that low sexual satisfaction was associated with health-related anxiety (33), something that has been documented; literature has highlighted the unfavorable relationship of anxiety and sexual contentment (80). Satisfaction deriving from sexual life is an integral part of sexual wellbeing and overall health (81). An important line of research has repeatedly shown that mentally healthy individuals are more satisfied by their intimate relationships, and vice versa; those with a more satisfying sex life exhibit a healthier mental state (80). However, the fact that some studies reported no change in satisfaction (49, 59) or other aspects of sexual wellbeing (48, 54) should not be neglected.

Based on the results, different aspects of sexual behaviors were found to have changed or to be newly added in individuals' lives. A significant increase was noted with respect to masturbation (52, 55, 60, 61, 67) and pornography use (58, 61, 65, 66). An plausible explanation for this increase could be the fact that pornography has been found to be utilized as a stress coping method (82), or as a means to avoid emotional burden (83). However, the reliability of these

findings should be considered carefully, as higher frequency of masturbatory practices appear more in males than females (84), and some of these studies have included solely male participants in their samples, while some samples constituted mostly by males. In addition, increases were reported with respect to online sexual activities such as cybersex, virtual dating, and creating and sharing sex-related digital content. Indeed, statistics on the topic has revealed the increase in dating applications' downloads (85). Given that during the pandemic initiating new intimate relationships could be perceived as "unsafe," virtual dating applications might offer a "safer" way to establish an alternative form of connection. It appears as intimacy quickly evolved and grew through online spaces, from emotional bonding *via* applications (86) to sex parties held *via* Zoom (87).

A wide heterogeneity was noted across studies. Each was conducted at different time points with respect to the severity of the pandemic. For example, a number of studies were conducted in countries with high number of infections and life losses, whereas in others -such as the example of Greece- studies were conducted when only a few cases of COVID-19 were being reported on a daily basis. Thereby, the impact of the pandemic could be characterized nothing but greatly variant. Thus, the implemented measures of social distancing were different when each study was conducted. For example in some European countries where the pandemic wave was milder restrictions were limited solely to the number of individuals that could gather, whereas in other countries complete ban of circulation was implemented. Another explanatory factor of the high heterogeneity could be the diverse samples between studies. Sampling varied significantly with respect to size, and demographic characteristics. Some included as small samples as of a few dozens of participants, while others recruited larger samples. In addition, both between and within studies sampling varied regarding gender, and relationship status; some included solely heterosexual or nonheterosexual participants, others included solely females or solely males, while others recruited mixed samples. The same issue occurred with respect to relationship status; some recruited exclusively married/cohabiting partners, while others solely single participants. The "when" and "how" is of great importance, as they could be the key factors in understanding the discrepancy of the findings.

Strengths and limitations

Among the strengths of the present study is the systematic approach of the available data, including the search strategy, the selection process, as well as the extraction and presentation of information. The explicit eligibility criteria ensured the exclusion of misleading factors, such as established sexual

or mental disorders prior the pandemic, while the data analysis assisted in the identification of trends between the included studies.

However, this review bears certain limitations. Though there was an effort to evaluate the impact of the stressful conditions formed by the pandemic on the sexual wellbeing and sexual behavior of individuals, specific factors limit the generalization of the findings. The fact that al included studies recruited convenient samples *via* online platforms constitute their findings vulnerable to selection and non-response biases, particularly regarding sexual behavior data. The meta-analysis was conducted on a small number of studies (especially for the male participants), which did not perform power calculation for their sample sizes, and thereby, their findings could be characterized as questionable. In addition, given the fact that a meta-regression could not be conducted, the mediating effect of other factors could not be determined.

Conclusion

COVID-19 has forced circumstances such as limitation of the usual social connection and, in some cases, the sense of constant life threat (88), which mental health professionals should take into consideration when treating patients. They must be prepared to desensitize mental health patients regarding irrational fears deriving from the pandemic. In addition, the higher risk of mental health complication for individuals with pre-existing mental conditions should be under consideration (89). In relation to COVID-19 preventive measures and restrictions, sexual well-being seems to have been negatively influenced across several domains. As it appeared, the state of anxiety and stress could be considered as the key explanatory factor; those with experiencing stronger distress due to the restrictive measures seemed to have a less satisfying sexual life. Simultaneously, a rise in specific internet-based sexual behaviors such as pornography use, and cybersex were also prominent as alternative ways of sexual relief. Given that sexual health is an integral part of general health, this paper's findings highlight that when the pandemic is surpassed and individuals begin to heal from this traumatic experience, surveillance and measurement of the final imprint on sexual wellbeing should be on the focus of clinicians and researchers.

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Data availability statement

The original contributions presented in this study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

IM designed the study. IM and IK conducted the search and study selection and drawn the first draft of the manuscript. EK-M and KK extracted the data. IK performed the meta-analyses. GK and CP conducted the review and editing. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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