EPIDEMIOLOGY/RISK FACTORS

Sexual Dysfunction in Infertile Men: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: According to previous studies of male infertility, we found that the association between sexual dysfunction and male infertility was reported rarely and controversially.

Aim: We carried out this 1meta-analysis to evaluate the prevalence of sexual dysfunction and the International Index of Erectile Function (IIEF) score in infertile men.

Methods: A systematic search of the target literature was conducted using PubMed, EMBASE, and Cochrane Library. Data were analyzed using Review Manager 5.4 software. Standardized mean differences (SMD) with the corresponding 95% confidence intervals (95% CIs) were implemented in 6 controlled studies as a measure of effect size to assess the relationship between sexual dysfunction and male infertility and Odds Ratio (OR) were performed for the morbidity between infertility group and fertility group.

Outcomes: Men in infertile group were found with higher prevalence of sexual dysfunction and lower IIEF values than in controls.

Results: A meta-analysis of morbidity was performed in 8 of 10 controlled studies. Meta-analysis of the 8 studies found remarkable higher prevalence of sexual dysfunction in men with infertility than in controls (OR = 2.66, 95% confidence interval = 1.69−4.19, $P < .0001$; $I^2 = 67\%$, P for heterogeneity = 0.004). Another meta-analysis of evidence suggested that IIEF in infertile men was lower than controls (SMD = −0.47, 95% confidence interval = −0.63 to −0.31, $P < .00001$; $I^2 = 64\%$, p for heterogeneity = 0.02).

Clinical Implications: We recommend further research based on the relevant criteria of region, sample size, rigorous statistical analysis, and research design.

Strengths & limitations: This systematic review is the first to evaluate the prevalence of sexual dysfunction and the score of sexual dysfunction in male infertility. Investigation on the topic is scarce, and only few studies used appropriate measures.

Conclusions: Male infertility was associated with an increase in the prevalence of sexual dysfunction. The areas most affected by sexual function were erectile function, orgasm and sexual desire. **Liu Y, Wang Y, Dong C, et al. Sexual Dysfunction in Infertile Men: A Systematic Review and Meta-Analysis. Sex Med 2022;10:100528.**

Key Words: International Index of Erectile Function; Sexual Dysfunction; Infertility; Men

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INTRODUCTION

Infertility is defined as unprotected intercourse within 1 year but still not pregnant.[1] About half of the cases involve male factors.[1] Infertility has been defined by the World Health Organization as a public health problem.[2] A large-scale epidemiological survey of the World Health Organization found that about half of couples are infertile due to simple or comprehensive male

factors. In addition, a 2013 study evaluated 22,682 interviews with men and women aged 15−44 and reported that as many as 12% of men in the United States have fertility problems.[3] As we all know, the diagnosis of infertility can cause psychological distress between husband and wife.[4] In addition, infertility can also lead to a decline in personal confidence and self-esteem; they are under treatment-related pressure, and despite the desire to have children, they still cannot get pregnant. Infertility can have a negative impact on the relationship between couples and usually causes sexual dissatisfaction.[4] Infertile men will bear a heavy psychological burden, so infertility and related psychological problems may be the main cause of sexual dysfunction.

Male sexual dysfunction is present in the general population, and 20−30% of adult men worldwide report at least one type of sexual dysfunction[5,6] and prevalence increase with increased age.[6] Erectile dysfunction and premature ejaculation are common types of male sexual dysfunction, but, only a few studies[7−9] have investigated erectile dysfunction and premature ejaculation in infertile men using proven methods, reporting a higher frequency of erectile dysfunction[7−9] and a similar[8,9] or higher[7] prevalence of premature ejaculation in the men of an infertile couple, compared with what is observed in the general male population of a similar age.

International Index of Erectile Function (IIEF/IIEF-15)[10] is a 5-dimensional scale for self-assessment of all male sexual functions within the past 4 weeks.[10,11] The use of IIEF is a recommended standard for the diagnosis and evaluation of erectile dysfunction.[11−13] The IIEF questionnaire consists of 15 items, divided into 5 collective domains (subscales) describing: I erectile function, II orgasm, III sexual desire, IV intercourse satisfaction, and V overall satisfaction.[10−12] The total scores within domains I−V create a positive dependence with correct sexual functioning.[10,11] Additional analysis of the erectile function subscale helps to distinguish the 4 different levels of erectile dysfunction (ED): normal erectile function (26−30 points), mild ED (17−25 points), and moderate ED (11−16 points) and severe ED (6−10 points). Clinically significant erectile dysfunctions are diagnosed at values of 25 points (cut-off point) or less.[12]

IIEF-5 evaluates the three aspects of penile erection function, namely vaginal insertion, erection maintenance, completion of intercourse, and overall satisfaction with sexual life and the patient's confidence in penile erection and maintenance. It has 5 items (factors) with the lowest possible score is 5 points, and the highest possible score is 25 points. The erectile function of the penis is divided into 5 levels according to the total score of IIEF-5: 5−7 are divided into severe erectile dysfunction (ED), 8−11 are divided into moderate ED, 12−16 are divided into moderate to mild ED, and 17−21 points are divided into mild ED. Twenty-two to 25 is classified as normal erectile function.[14,15] We acknowledge limitation of IIEF-5 as it only explores erectile function domains.

Therefore, the purpose of this study is to evaluate the severity of sexual dysfunction with the IIEF score and the prevalence of sexual dysfunction in infertile men. In view of the current literature gap, it is necessary to conduct a systematic review in this field to summarize the research on sexual dysfunction in infertile men and provide valuable information to clinicians and other relevant personnel dealing with reproductive and sexual health and infertility.

MATERIALS AND METHODS

This systematic review was developed rested upon the recommendations from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statements.[16] The protocol is registered in the PROSPERO registry (CRD42021272781, http://www.crd.york.ac.uk/PROSPERO).

Search Strategy

A systematic search in three available databases (PubMed, EMBASE, and Cochrane Library) was performed to identify all relevant studies published from January 2000 to September 2021, with no language restriction. We also analyzed related additional studies identified in the reference list of primary and event studies (Figure 1).

We used the following terms to retrieve in PubMed: ((((((((((“Infertility, Male”[Mesh])) OR (Male Infertility)) OR (Sterility, Male)) OR (Male Sterility)) OR (Subfertility, Male)) OR (Male Subfertility)) OR (Sub-Fertility, Male)) OR (Male Sub-Fertility)) OR (Sub Fertility, Male)) OR ((((((((((“Oligospermia”[Mesh]) OR (Hypospermatogenesis)) OR (Hypospermatogeneses)) OR (Low Sperm Count)) OR (Low Sperm Counts)) OR (Sperm Count, Low)) OR (Sperm Counts, Low)) OR (Oligoasthenoteratozoospermia)) OR (Oligoasthenoteratozoospermias)) OR (Oligozoospermia))) OR (“Azoospermia”[Mesh])) AND ((((((((((“Sexual Dysfunction, Physiological”[Mesh]) OR (Physiological Sexual Dysfunction)) OR (Physiological Sexual Dysfunctions)) OR (Sexual Dysfunctions, Physiological)) OR (Sexual Disorders, Physiological)) OR (Physiological Sexual Disorder)) OR (Physiological Sexual Disorders)) OR (Sexual Disorder, Physiological)) OR (Sex Disorders)) OR (((((((“Erectile Dysfunction”[Mesh]) OR (Dysfunction, Erectile)) OR (Male Sexual Impotence)) OR (Impotence, Male Sexual)) OR (Sexual Impotence, Male)) OR (Male Impotence)) OR (Impotence, Male)) OR (Impotence))) OR (((((((“Premature Ejaculation”[Mesh]) OR (Ejaculation, Premature)) OR (Ejaculations, Premature)) OR (Premature Ejaculations)) OR (Ejaculatio Praecox)) OR (Ejaculatio Praecoxs)) OR (Praecox, Ejaculatio)) OR (Praecoxs, Ejaculatio))). Manipulated the following filter: publication dates from January 2000 to September 2021, excluding reviews and systematic reviews. This same combination of words was used to search in Cochrane Library.

We used the following terms to retrieve in EMBASE: (‘infertility’/exp OR (‘fertility disorder’:ab,ti OR infecundity:ab,ti OR ‘primary infertility’:ab,ti OR ‘secondary infertility’:ab,ti OR ‘sexual sterility’:ab,ti OR ‘sterility, sexual’:ab,ti) OR ‘oligospermia’/

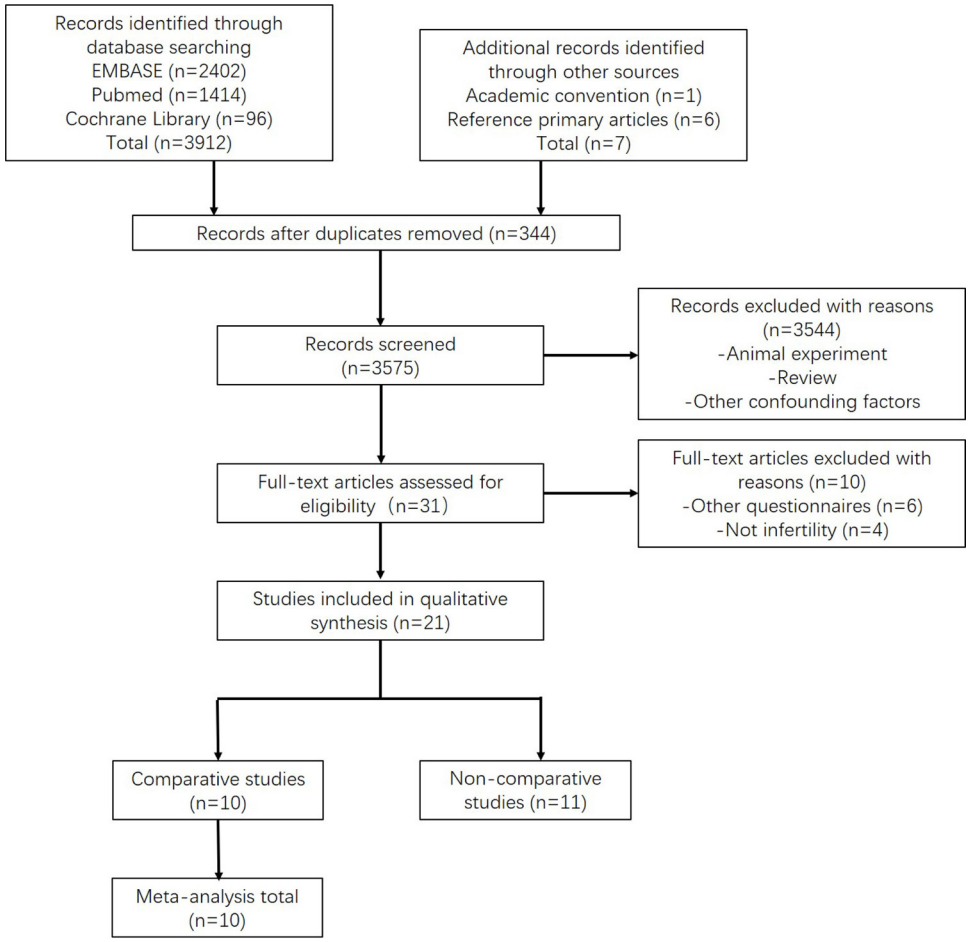

Figure 1. Flow diagram.

exp OR (hypospermia:ab,ti OR oligoasthenospermia:ab,ti OR oligoasthenospermy:ab,ti OR oligospermy:ab,ti OR oligozoospermia:ab,ti))AND ('sexual dysfunction'/exp OR ('dysfunction, sexual':ab,ti OR 'physiological sexual dysfunction':ab,ti OR 'sex abnormality':ab,ti OR 'sex disorders':ab,ti OR 'sex dysfunction':ab,ti OR 'sex insufficiency':ab,ti OR 'sex problem':ab,ti OR (sexual:ab,ti AND 'gender disorders':ab,ti) OR 'sexual asthenia':ab,ti OR 'sexual disability':ab,ti OR 'sexual disorder':ab,ti OR 'sexual disturbance':ab,ti OR 'sexual dysfunction, physiological':ab,ti OR 'sexual problem':ab,ti) OR 'erectile dysfunction'/exp OR 'dysfunction, erectile':ab,ti OR 'international index of erectile function'/exp)AND ('male'/exp OR (males:ab,ti OR man:ab,ti OR men:ab,ti)).

Eligibility Criteria

The inclusion criteria for this study were as follows: (i) studies measuring male sexual dysfunction in infertile couples; (ii) studies reporting total score of IIEF/IIEF-5 or its domains individually or studies describing the prevalence and average value of sexual dysfunction; (iii) observational studies (cross-sectional, case-control, or cohort) including controlled studies (infertile vs fertile men) and noncontrolled studies (including infertile men only); and (iv) studies on men diagnosed with infertility due to simple male factors, couple factors, or unknown reasons who were receiving human reproduction treatment at the time of data collection. Included studies were required to meet all of the above criteria. In addition, when the total IIEF score was <26 or the total IIEF-5 score was <22, the sexual dysfunction was determined. We excluded articles (i) that used other questionnaires or questionnaires that were not clearly identified to measure male sexual function to evaluate male sexual function; (ii) that were case reports; (iii) that evaluated diseases other than infertility; (iv) that failed to mention sexual dysfunction in infertility men, or infertility and sexual function in children and adolescents; and (v) that could not get meaningful data for this review even after we contacted the authors via e-mail.

Study Selection, Data Extraction, and Quality of Evidence

Read the titles of all articles retrieved from the database search. Examined abstracts of relevant articles on the relationship between the surveys, and searched all studies that might be included in this review, regardless of population size, source, or age. The included articles were reviewed by two researchers.

Extracted data that met the purpose of the research and resolved differences through consensus. All closely related literature, meta-analysis, and review articles were also reviewed for their reference lists to identify additional published work not indexed by above-mentioned databases. Disagreements about whether a study should be included were addressed by a third reviewer. The data collected were as follows: authors and publication year, type of study, country, sample size, age, mean, and standard deviation (SD) of IIEF score and 5 subfields, and male prevalence of sexual dysfunction. Data for controlled and non-controlled studies were collected separately. Other information was obtained by contacting authors via e-mail. We used Newcastle Ottawa Scale (NOS)[17] to evaluate the quality of included case-control studies and the Agency for Healthcare Research Quality (AHRQ) to evaluate the inclusion of cross-sectional studies. The highest score for NOS was 9 points. Studies with an NOS score between 5 and 7 and greater than 7 were considered "medium"-quality studies and "high"-quality studies, respectively. On the contrary, studies with NOS score lower than 5 points were considered "low"-quality studies. We also analyzed the impact of possible conflicts of interest and whether the research was ethically approved.[18]

Statistical Analysis

Statistical analyses were executed using REVMAN(Review Manager)5.4 software. We used mean ± standard (SD) to extract IIEF values from each included study. Due to the different measurement methods of the IIEF among studies, we used standardized mean difference (SMD) and the corresponding 95% confidence interval (CI) as a measure of effect size to evaluate the value of IIEF between the control group and the infertile group. Statistical significances were obtained using the x^2 test and the pooled effect was considered significant when $P < .05$. The percentage of variability across studies attributable to heterogeneity was estimated using the I^2 test, which was considered to be a significant difference when $P < .05$. I^2 values of 25%, 50%, and 90% corresponded to low, medium, and high levels of heterogeneity, respectively. The random effects model was used to merge data due to excessive heterogeneity. Subgroup analysis and sensitivity analysis were also performed to explore the sources of heterogeneity between studies. We observed the funnel plot to assess whether there was publication bias.

RESULTS

Included Studies

The search strategy identified a total of 1677 articles. We completely read 31 articles with titles and abstracts that met the requirements, 6 studies using different questionnaires to investigate sexual function, and 4 studies without infertility data were excluded. Finally, 21 articles were included in the scope of the analysis, of which 10 were controlled studies (Figure 1). Three studies conducted in Turkey[19–21]; 3 studies in China[7,22,23]; 2 studies in Italy[8,24]; 1 study in USA[25] and 1 study in Poland.[26]

These studies included men of different ages and races and from different countries and regions. Infertility diagnosis was divided into a simple male factor group and a 2-sided or unexplained factor group. The experimental group of some studies was infertility caused by pure male factors,[7,8,19,21,22] while the experimental group of other studies was infertility caused by 2-sided or unexplained factors.[23–26] In addition, some studies reported the frequency of sexual dysfunction,[7,8,20–24,26] and others reported the mean IIEF score.[7,20,22,23,26]

Prevalence of Sexual Dysfunction in Infertile Men

According to controlled studies, infertile men had a higher prevalence of sexual dysfunction. For most studies, there were significant differences in characteristics between infertile men and fertile men (Table 1). Of 11 noncontrolled studies, 7 reported data on the prevalence of sexual dysfunction in infertile men (Table 2).[7,8,20,23–26] The prevalence of sexual dysfunction in infertile men ranged from 17.8% to 61.6%.

Meta-Analysis

Meta-analysis of the prevalence of sexual dysfunction was performed in 8 controlled studies[7,8,20–24,26]; 2 studies had no relative data and were thus excluded.[19,25] The infertile group consisted of 3,243 men, and the fertility group consisted of 1,555 people. The results showed that there was a significant association between male sexual dysfunction and infertility (OR = 2.50, 95% confidence interval = 2.07−3.01, $P < .00001$), and there was a high degree of heterogeneity between studies (I^2 = 67%, $P = .004$). Therefore, we chose a random effects model for analysis (OR = 2.66, 95% confidence interval = 1.69−4.19, $P < .0001$; Figure 2). There was a significant difference in the IIEF value between the two groups (SMD = −0.47, 95% confidence interval = −0.63 to −0.31, $P < .00001$), and high heterogeneity between studies was noted (I^2 = 64%, $P = .02$; Figure 3). Subsequently, subgroup analysis found that the diagnosis of infertility (simple male factor vs 2-sided factors) was not the cause of heterogeneity.

We also performed a meta-analysis of individual IIEF domains in 6 studies.[19–21,24–26] Four studies were not able to obtain data on individual IIEF domains,[7,8,22,23] even after we contacted the authors, and thus were excluded. Results based on random effects model showed that infertile men had problems with erectile function (SMD = −0.29, 95% CI = −0.53 to −0.05, $P = .02$) (I^2 = 69%, P for heterogeneity = 0.007; Figure 4), orgasm (SMD = −0.48, 95% CI = −0.95 to −0.01, $P = .04$; I^2 = 82%, P for heterogeneity = 0.004; Figure 5), and sexual desire (SMD = −0.68, 95% CI = −1.20 to −0.15, $P = .01$; I^2 = 85%, P for heterogeneity = 0.001; Figure 6), and high evidence of heterogeneity was observed. Meanwhile, we conducted a sensitivity analysis on the results of erectile function and excluded a study[25] from the scope of

Table 1. Characteristics of the controlled studies on sexual dysfunction in infertile and fertile men in the systematic review

Author	Country	Study design	Quality score	Conflict of interest	Ethics committee approval	Infertility Diagnostic	Sample size,number		Age		Erectile dysfunction prevalence		P	IIEF-5(0-25)		P	IIEF-15		P
							Infertile	Fertile	Infertile	Fertile	Infertile	Fertile		Infertile	Fertile		Infertile	Fertile	
Kızılay et al. (2017)	Turkey	Cross-sectional	5[a]	No	Yes	Male infertility	98	81	33.75 ± 3.46	34.99 ± 3.46									
Ozkan et al. (2015)	Turkey	Case-control	8[b]	No	Yes	Male infertility	56	48	33.9 ± 5.1	35.6 ± 3.7	84.9%	100%	>0.05				45.7 ± 7.5	50.4 ± 3.2	
Gao et al. (2013)	China	Cross-sectional	10[a]	No	Yes	Male infertility	1468	942	28.47 ± 6.29	27.92 ± 7.03	18.05%	8.28%	0.001	21.24 ± 6.17	23.28 ± 4.25	0.012			
Drosdzol et al. (2008)	Poland	Cross-sectional	7[a]	No	Yes	Infertile couples	188	190	31.4 ± 4.7	32.8 ± 6.5	23.9%	13.7%					66.5 ± 8.9	68.4 ± 5.7	
Lotti et al. (2016)	Italy	Cross-sectional	7[a]	No	Yes	Male infertility	448	74	36.8 ± 7.9	36.2 ± 5.0	18.3%	0%	0.006						
Pan et al. (2013)	China	Cross-sectional	7[a]	No	Yes	Infertile couples	245	52	31 ± 4.1		50.61%	15.38%	<0.01	21.24 ± 2.58	23.21 ± 1.61				
Ma et al. (2017)	China	Cross-sectional	6[a]	No	Yes	Male infertility	245	97	33.1 ± 4.9	33.0 ± 5.1	28.6%	12.4%	0.002	21.4 ± 3.9	23.2 ± 3.1	0.001			
Marci et al. (2012)	Italy	Case-control	7[b]	No	Yes	Infertile couples	30	52	38.53 ± 2.87	37.30 ± 3.45	26.6%	0%							
Monga et al. (2004)	U.S.	Cross-sectional	5[a]	No	Yes	Infertile couples	18	12	35 ± 4.25										
Canyan et al. (2015)	Turkey	Cross-sectional	5[a]	No	Yes	Male infertility	563	100	32.55 ± 6.12	32.34 ± 6.77	42.7%	28%							

IIEF = International Index of Erectile Function.
[a]The Agency for Healthcare Research and Quality was used for quality scoring in the included studies.
[b]The Newcastle Ottawa Scale was used for quality scoring in the included studies.

Table 2. Characteristics of the noncontrolled studies on sexual dysfunction in infertile men included in the systematic review

Author	Country	Study design	Conflictof interest	Ethicscommittee approval	Infertility Diagnostic	Patients number	Age	Erectile dysfunction prevalence	IIEF-5(0-25)	IIEF-15
Mazzilli et al. (2020)	Italy	cross-sectional	No	Yes	male infertility	3280	NA			
Yıkılmaz TN et al. (2019)	Turkey	cross-sectional	No	Yes	infertile men with non-obstructive azoospermia	193	31 ± 4.2	35.2%	16	
Lotti et al. (2012)	Italy	cross-sectional	No	Yes	Couple Infertility	244	35.2 ± 7.8	17.8%		
Song et al. (2016)	Korea	cross-sectional	No	Yes	male partners of infertile couples	236	38.5	51%		
Khademi et al. (2008)	Iran	cross-sectional	No	Yes	Infertile Couples	100	32.3 ± 5.3	61.6%		
Shindel et al. (2008)	America	cross-sectional	No	Yes	Infertile Couples	121	35 ± 7	22%		65.9 ± 10.1
Pasha et al. (2020)	Iran	cross-sectional	No	Yes	Infertile Couples	204	31.77 ± 5.47			58.30 ± 8.52
Yang et al. (2018)	China	cross-sectional	No	Yes	Infertile Couples	4299	32.85 ± 5.98	57.8%		
Ma et al. (2021)	China	cross-sectional	No	Yes	Infertile Couples	387	33.9 ± 5.7	33.3%	21.2 ± 3.9	
Coward et al. (2019)	America	cohort	No	Yes	Infertile Couples	708	34.2 ± 5.6			
2Shindel et al. (2008)	America	cross-sectional	No	Yes	Infertile Couples	73	34 ± 7			68.1 ± 7.3

IIEF = International Index of Erectile Function.

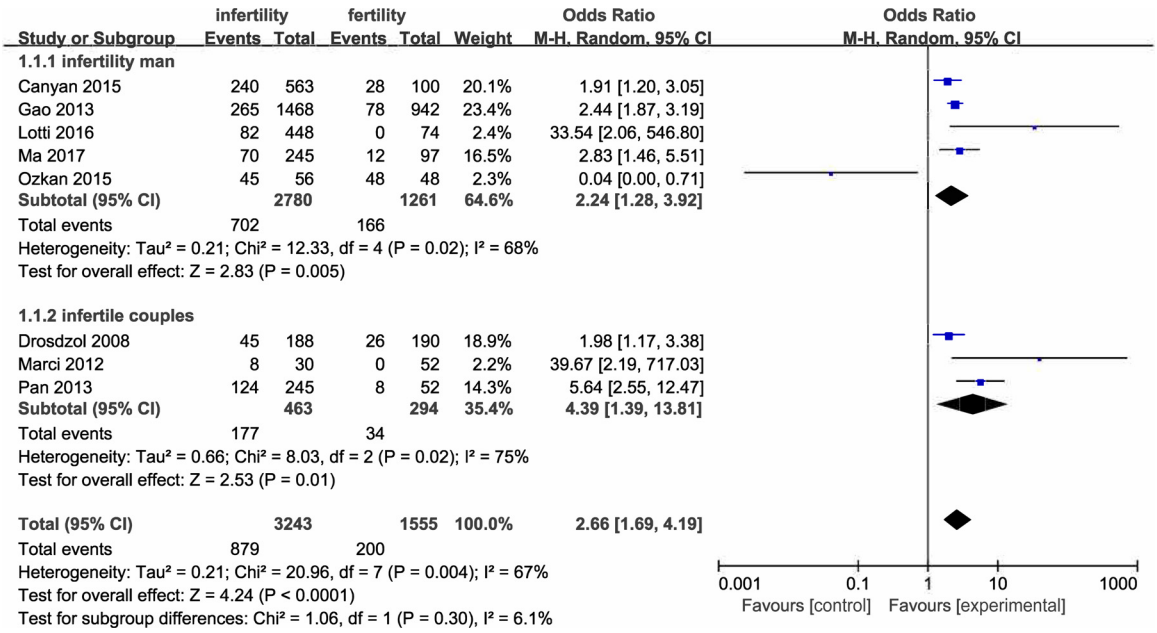

Figure 2. Results of the meta-analysis for the prevalence of sexual dysfunction.

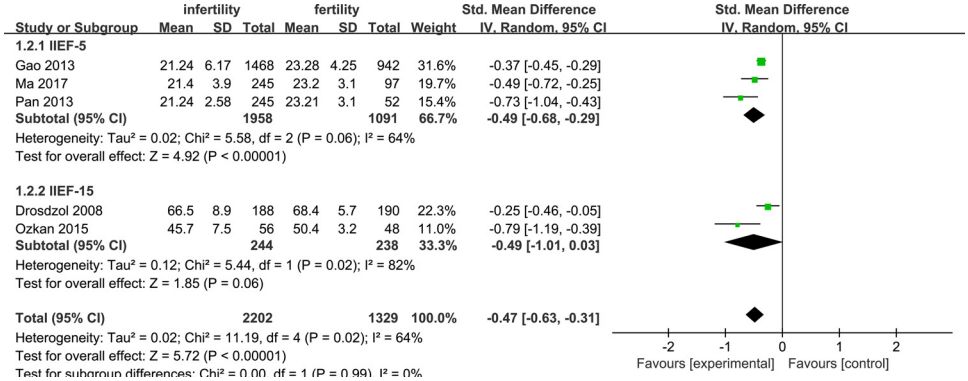

Figure 3. Results of the meta-analysis for total IIEF score controlled studies.

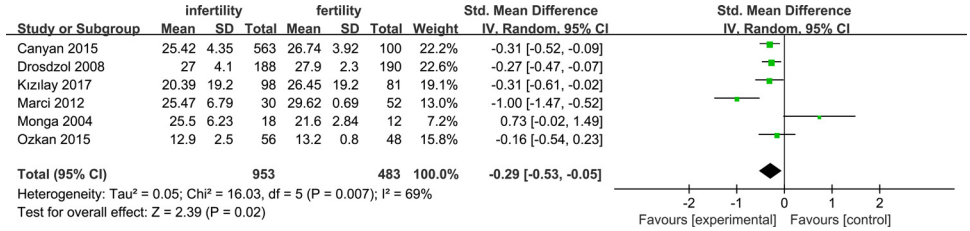

Figure 4. Results of the meta-analysis for erectile function.

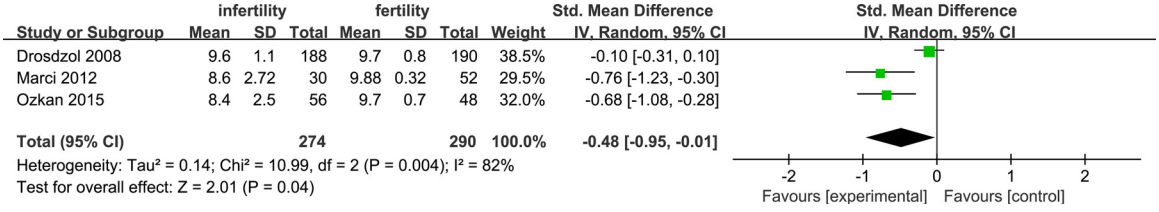

Figure 5. Results of the meta-analysis for orgasm.

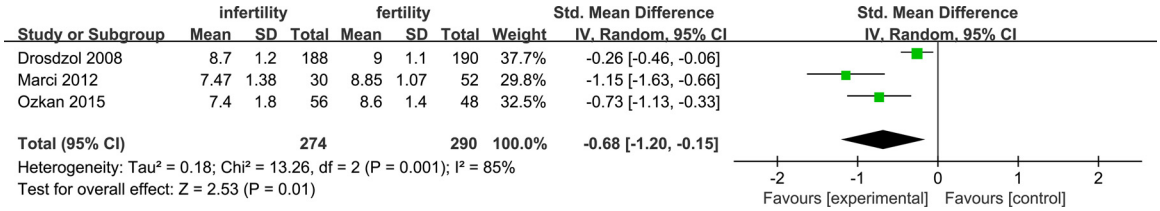

Figure 6. Results of the meta-analysis for sexual desire.

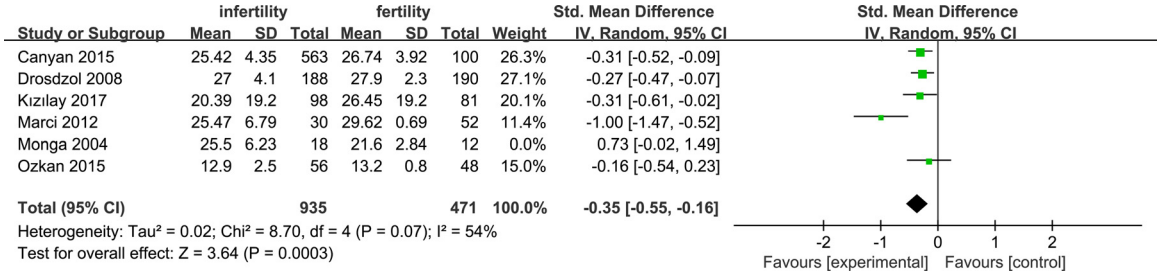

Figure 7. The sensitivity analysis on erectile function.

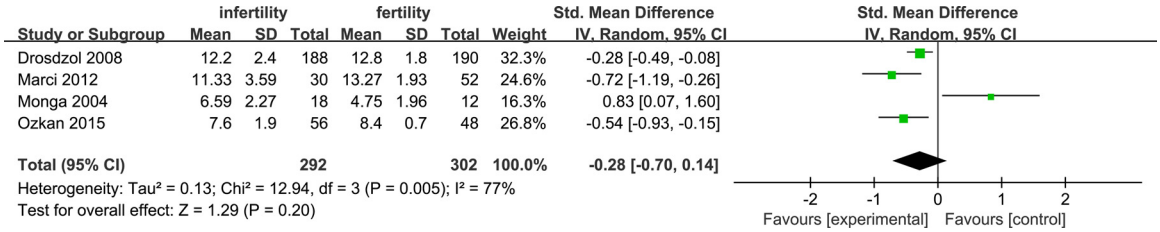

Figure 8. Results of the meta-analysis for intercourse satisfaction.

analysis, and the results showed a significant decrease in heterogeneity (SMD = −0.35, 95% CI = −0.55 to −0.16, P = .0003; I^2 = 54%, P for heterogeneity = 0.07) (Figure 7).

The results of the meta-analysis indicated that infertility was not associated with intercourse satisfaction (SMD = −0.28, 95% CI = −0.70 to 0.14, P = .20; I^2 = 77%, P for heterogeneity = 0.005; Figure 8), and overall satisfaction (SMD = −0.33, 95% CI = −0.66 to 0.01, P = .06; I^2=66%, P for heterogeneity = 0.05; Figure 9). Due to the small number of included studies, the conclusion may be changed based on the addition of related studies.

Heterogeneity Analysis

Heterogeneity analysis includes subgroup analysis and sensitivity analysis. We conducted a subgroup analysis on the prevalence of sexual dysfunction and divided it into a pure male factor infertility group and a 2-factor infertility group. The results showed that this grouping factor was not a source of heterogeneity, but we found that the 2-factor infertility group (OR = 4.39) is more likely to cause male sexual dysfunction than pure male factor group (OR = 2.24). We also conducted a sensitivity analysis on the prevalence of sexual dysfunction, and excluded a study[20] from the scope of analysis, and the results showed a decrease in heterogeneity (SMD = 2.78, 95% CI = 1.91−4.04, P < .00001; I^2 = 56%, P for heterogeneity = 0.04; Figure 10).

We also conducted a subgroup analysis on the value of IIEF and divided it into an IIEF-5 group and an IIEF-15 group. The results showed that this grouping factor was not a source of heterogeneity.

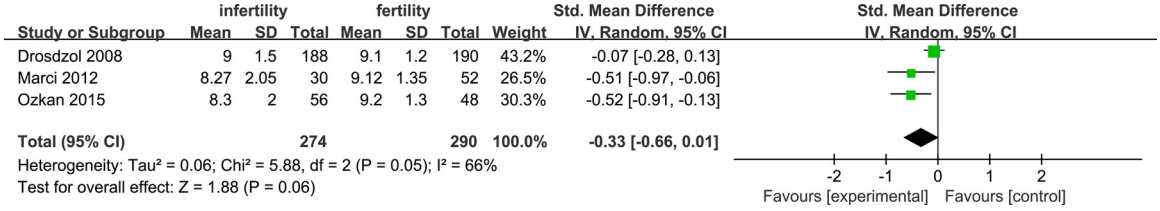

Figure 9. Results of the meta-analysis for overall satisfaction.

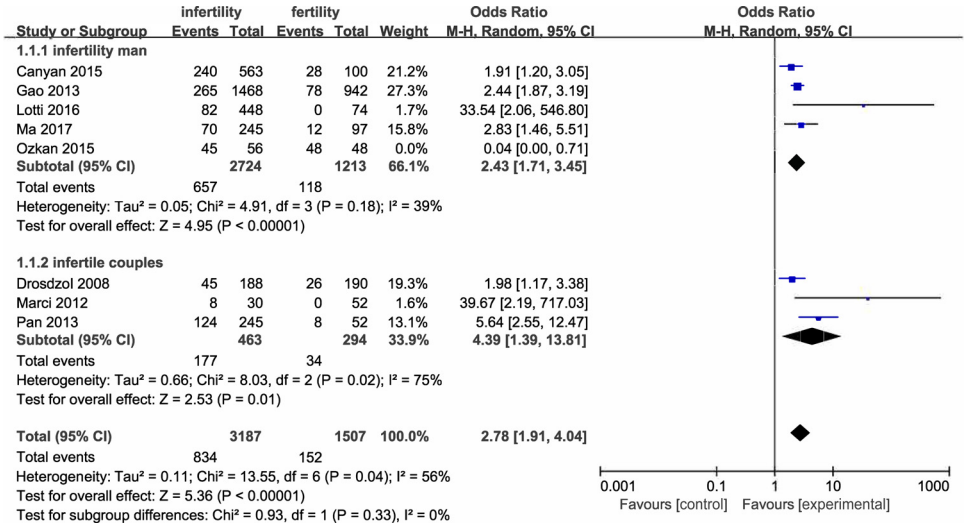

Figure 10. The sensitivity analysis on the prevalence of sexual dysfunction.

Publication Bias

The funnel plot showed that the graph is symmetrical, which indicated that there was no publication bias in our meta-analysis (Figure 11). The quality scores of included case-control studies ranged from 7 to 8 (Table 3), and cross-section studies scored from 5 to 10 (the maximum AHRQ score was 11, low quality: 1−3, moderate quality: 4−7, high quality: 8−11) (Table 4). Analysis of the methodological quality of the studies performed using NOS and AHRQ indicated moderate to high quality, which is expected in observational studies. All studies received ethical approval, and there was no conflict of interest between the authors.

DISCUSSION

This systematic review is the first to evaluate the prevalence of sexual dysfunction and the score of sexual dysfunction in male infertility. Although infertility and its impact on male sexual function are not new, the results of most existing studies are contradictory, and the methods of evaluating sexual function are not uniform, prompting us to conduct a systematic review. The results of the meta-analysis confirmed that male infertility was associated with an increase in the prevalence of sexual dysfunction. The most affected sexual function domains were erectile function, orgasm, and sexual desire domains

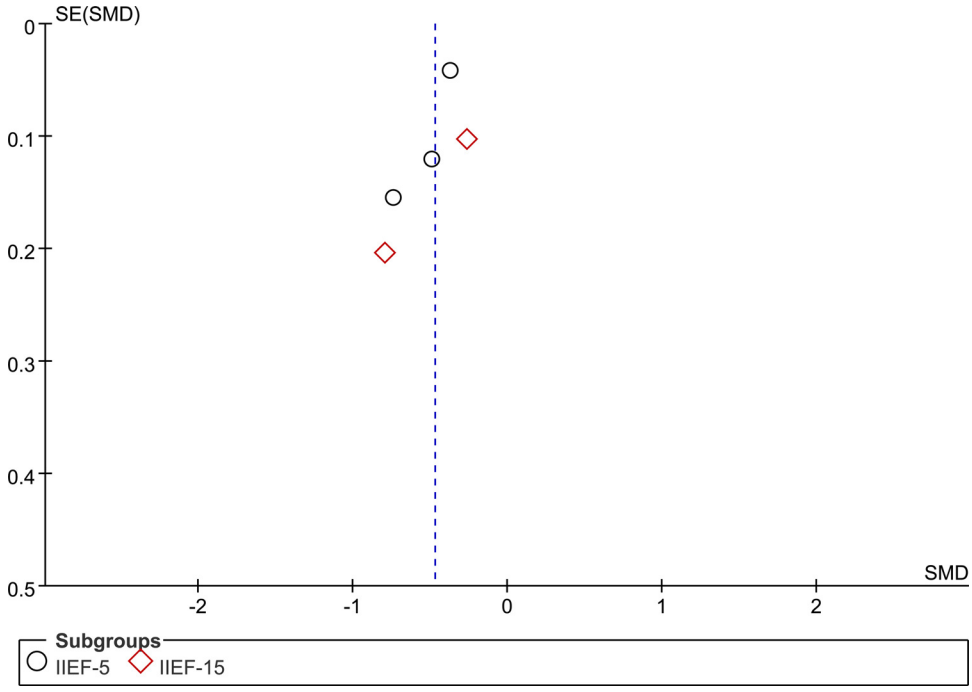

Figure 11. Funnel plot of the controlled studies.

Table 3. The quality of included case-control studies performed using NOS

	Selection					Exposure			
Study	Adequate definition of cases	Representativeness of the cases	Selection of controls	Definition of controls	Comparability control for important factor	Ascertainment of exposure	Same method of ascertainment for cases and controls	Nonresponse rate	Scores
Ozkan et al.(2015)	☆	☆	☆	☆	☆☆	☆	☆		8
Marci et al.(2012)	☆	☆	☆	☆	☆	☆	☆		7

Table 4. The quality of included cross-section studies performed using AHRQ

	Kızılay et al. (2017)	Gao et al. (2013)	Drosdzol et al. (2008)	Lotti et al. (2016)	Pan et al. (2013)	Ma et al. (2017)	Monga et al. (2004)	Canyan et al. (2015)
Define the source of information	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
List inclusion and exclusion criteria for exposed and unexposed subjects (cases and controls) or refer to previous publications	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Indicate time period used for identifying patients	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Indicate whether or not subjects were consecutive if not population-based	No	Yes	No	Unclear	No	No	No	Unclear
Indicate if evaluators of subjective components of study were masked to other aspects of the status of the participants	No	No	NO	No	No	No	No	Unclear
Describe any assessments undertaken for quality assurance purposes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Explain any patient exclusions from analysis	No	Yes	Yes	Yes	Yes	No	No	Unclear
Describe how confounding was assessed and/or controlled	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
If applicated, explain how missing data were handled in the analysis	Unclear	Yes	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Summarize patient response rates and completeness of data collection	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear
Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained	Unclear	Yes	Unclear	No	No	No	No	Unclear
scores	5	10	7	7	7	6	5	5

Our findings are of great value and can provide new clinical ideas for professionals dealing with sexual and reproductive health; Evaluation and assisted treatment (ART) of infertility is an important risk factor for sexual dysfunction.[27–29] It is worth noting that infertility may adversely affect the sex life, psychology, and marriage of both spouses.[30,31] Other excluded studies reported on the influence of erectile dysfunction, premature ejaculation, hypoactive sexual desire disorder, satisfaction impairment, and orgasmic dysfunction in infertile men related to sexual dysfunction.[32–35]

Although we used subgroup analysis and sensitivity analysis to explore the source of heterogeneity, the results did not directly reflect the source of heterogeneity. The 10 controlled studies we included were performed in different regions, 4 from developed countries and 6 from developing countries. The sample sizes of different studies varied greatly, with the most[7] contained 2,410 samples and the least[25] were only 30 samples. Besides, the heterogeneity between studies may come from factors such as regional and cultural differences, age of participants, diagnosis of infertility, and the sample size.

This study has some limitations. First, due to the limited number of controlled studies on the sexual function of male infertility patients, this analysis did not include a sufficient number of studies. Second, some studies did not have complete data information. Third, differences in the control group may not be representative of the general population. The last limitation was the high heterogeneity of research. We recommend further research based on the relevant criteria of region, sample size, rigorous statistical analysis and research design. In addition, future studies should consider the age of men and the number of failed assisted reproductive treatments when interpreting the results.

An important feature of this review is the inclusion of articles that use IIEF as the outcome variable. In order to protect the privacy of patients, the evaluation of patients' sexual function was carried out through observational studies; therefore, we tried to obtain various relevant case-control, cohort and cross-sectional studies. The lack of data and the diversity of research require a careful and differentiated inspection. Checked the data carefully to minimize the risk of bias. Some validated methods were used to assess quality and risk of bias, namely funnel plot, NOS, and AHRQ. We also excluded studies with a potential risk of bias.

In our literature screening process, we found a large number of studies that reported infertile men with sexual dysfunction were accompanied by psychological symptoms such as anxiety and depression. Many otherwise healthy young men may be adversely affected by fertility pressure, leading to various sexual dysfunctions that affect fertility. The most common thing is that men will be affected by anxiety and depression and reduced pornographic cues during this process. It reminds future clinicians and experimenters to pay attention not only to men's physical health but also to their mental health. We also noted the obvious likely relationship between sexual dysfunction in infertile men when related to endocrinopathy like Klinefelter that may be a reasonable cause for both disorders.

Compared with the control group, the prevalence of sexual dysfunction in the infertile group was more common. Infertility clinicians involved in reproductive health and human sexuality should be aware of this problem in order to evaluate and treat patients to improve their quality of life, and seek to avoid problems that may arise during diagnosis and treatment. It is recommended to investigate the sexual function, general health and psychological status of men in infertile couples, especially young men with azoospermia, in order to improve reproductive health, general health and sexual health. Guidance and monitoring must start from the diagnosis of infertility to the end of the treatment period, including the process of assisted reproduction. Psychotherapy monitoring also helps to minimize the occurrence of sexual dysfunction and improve the patient's quality of life.[7] Therefore, providing couples with sexual dysfunction counseling and proposing treatment strategies can help improve their sexual and emotional relationships and increase the success rate of assisted reproductive treatments.

In conclusion, male infertility was associated with an increase in the prevalence of sexual dysfunction. The areas most affected by sexual function were erectile function, orgasm, and sexual desire.

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REFERENCES

1. Irvine DS. Epidemiology and aetiology of male infertility. **Hum Reprod 1998;13(Suppl 1):33–44.**
2. Boivin J, Bunting L, Collins JA, et al. International estimates of infertility incidence and treatment-seeking: Potential need and demand for infertility medical care. **Hum Reprod 2007;22:1506–1512.**
3. Chandra A, Copen CE, Stephen EH. Infertility and impaired fecundity in the United States, 1982-2010: Data from the National Survey of Family Growth. **Natl Health Stat Report 2013:1–18, 1 p following 9.**

4. Muller MJ, Schilling G, Haidl G. Sexual satisfaction in male infertility. **Arch Androl 1999;42:137–143.**
5. Berger MH, Messore M, Pastuszak AW, et al. Association between infertility and sexual dysfunction in men and women. **Sex Med Rev 2016;4:353–365.**
6. Lewis RW, Fugl-Meyer KS, Corona G, et al. Definitions/epidemiology/risk factors for sexual dysfunction. **J Sex Med 2010;7:1598–1607.**
7. Gao J, Zhang X, Su P, et al. Relationship between sexual dysfunction and psychological burden in men with infertility: A large observational study in China. **J Sex Med 2013;10:1935–1942.**
8. Lotti F, Corona G, Castellini G, et al. Semen quality impairment is associated with sexual dysfunction according to its severity. **Hum Reprod 2016;31:2668–2680.**
9. Lotti F, Corona G, Rastrelli G, et al. Clinical correlates of erectile dysfunction and premature ejaculation in men with couple infertility. **J Sex Med 2012;9:2698–2707.**
10. Rosen RC, Riley A, Wagner G, et al. The international index of erectile function (IIEF): A multidimensional scale for assessment of erectile dysfunction. **Urology 1997;49:822–830.**
11. Rosen RC, Cappelleri JC, Gendrano N. The International Index of Erectile Function (IIEF): a state-of-the-science review. **Int J Impot Res 2002;14:226–244.**
12. Cappelleri JC, Rosen RC, Smith MD, et al. Diagnostic evaluation of the erectile function domain of the international index of erectile function. **Urology 1999;54:346–351.**
13. Lue TF, Giuliano F, Montorsi F, et al. Summary of the recommendations on sexual dysfunctions in men. **J Sex Med 2004;1:6–23.**
14. ZHU J-c. Guidelines for the diagnosis and treatment of men's erectile dysfunction. **Chinese Journal of Andrology Vol 2004;18:68–72.**
15. Rosen RC, Cappelleri JC, Smith MD, et al. Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. **Int J Impot Res 1999;11:319–326.**
16. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. **J Clin Epidemiol 2009;62:e1–34.**
17. Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality if nonrandomized studies in meta-analyses. URL: http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm
18. Elia N, von Elm E, Chatagner A, et al. How do authors of systematic reviews deal with research malpractice and misconduct in original studies? A cross-sectional analysis of systematic reviews and survey of their authors. **BMJ open 2016;6:e010442.**
19. Kızılay F, Şahin M, Altay B. Do sperm parameters and infertility affect sexuality of couples? **Andrologia 2018;50.**
20. Ozkan B, Orhan E, Aktas N, et al. Depression and sexual dysfunction in Turkish men diagnosed with infertility. **Urology 2015;85:1389–1393.**
21. S C. Incidence of sexual dysfunction and effect of medical treatment for fertility on sexual functions in infertile men. **J Sex Med 2015;12:200.**
22. Ma J-X, Wang B, Dang J, et al. Erectile dysfunction and psychological status in infertile males. **Natl J Androl 2017;23:609–614.**
23. Pan B-C, Xing X, LI P, et al. Impact of perceived male infertility factors on penile erectile function. **Natl J Androl 2013;19:1087–1090.**
24. Marci R, Graziano A, Piva I, et al. Procreative sex in infertile couples: The decay of pleasure? **Health Qual Life Outcomes 2012;10:140.**
25. Monga M, Alexandrescu B, Katz SE, et al. Impact of infertility on quality of life, marital adjustment, and sexual function. **Urology 2004;63:126–130.**
26. Drosdzol A, Skrzypulec V. Quality of life and sexual functioning of Polish infertile couples. **Eur J Contracept Reprod Health Care 2008;13:271–281.**
27. Piva I, Lo Monte G, Graziano A, et al. A literature review on the relationship between infertility and sexual dysfunction: Does fun end with baby making? **Eur J Contracept Reprod Health Care 2014;19:231–237.**
28. Ciocca G, Limoncin E, Mollaioli D, et al. SIAMS survey on sexological screening during the assisted reproductive technologies in Italy. **J Endocrinol Invest 2015;38:999–1005.**
29. Lenzi FL A, Salacone P, Gandini L, et al. Stress, sexual dysfunctions, and male infertility. **J Endocrinol Invest 2003;26:72–76.**
30. Ferraresi SR, Lara LA, de Sa MF, et al. Current research on how infertility affects the sexuality of men and women. **Recent Pat Endocr Metab Immune Drug Discov 2013;7:198–202.**
31. Lara LA, Salomao PB, Romao AP, et al. Effect of infertility on the sexual function of couples: State of the art. **Recent Pat Endocr Metab Immune Drug Discov 2015;9:46–53.**
32. Berger DM. Impotence following the discovery of azoospermia. **Fertil Steril 1980;34:154–156.**
33. Berger DM. Couples' reactions to male infertility and donor insemination. **Am J Psychiatry 1980;137:1047–1049.**
34. Zyl JAv. Sex and infertility. Part I. Prevalence of psychosexual problems and subjacent factors. **S Afr Med J 1987;72:482–484.**
35. Jain GR K, Agrawal P. Infertility and psychosexual disorders: Relationship in infertile couples. **Indian J Med Sci 2000;54:1–7.**