

# Sexual dysfunction in polycystic ovary syndrome: a systematic review and meta-analysis

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### **Abstract**

Background Polycystic ovarian syndrome is a common disorder characterized by clinical or biochemical hyperandrogenism and ovulary dysfunction. Female sexual dysfunction can have adverse effects on quality of life and interpersonal relationship. Methods We conducted a meta-analysis to evaluate the prevalence and severity of sexual dysfunction in women with PCOS. Results Compared to women without PCOS, those with PCOS were younger (28.90±3.11 versus 31.42±3.37 years; p<0.0001) and had higher body mass index (27.76±3.79 versus 24.95±3.71 kg/m2; p=0.002), Ferriman-Gallwey score (9.90±3.37 versus 4.11±2.17; p<0.0001) and serum total testosterone level (2.26±0.59 versus 1.51±0.49 nmol/L; p<0.0001). There was no significant difference in mean total FSFI score (25.72±2.33 versus 26.62±3.38; p=0.608) in women with and without PCOS. For the FSFI subscales, women with PCOS had a lower score for the pain subscale than women without PCOS (4.60±0.71 versus 5.24±0.39; p<0.001). Other subscales were not significantly different between the two groups. Women with PCOS had a 1.39 higher odds (95% Cl 1.13, 1.72; p=0.002, l2 11.9%) of having FSD than women without PCOS. Conclusion FSD is a prevalent and disabling condition in young women with PCOS. Sensitive probing into the intimate aspects of their sex lives is needed to further understand the struggles that afflict women with PCOS. Parallel efforts should be undertaken to investigate the impact of new treatment strategies.

## Introduction

Polycystic ovary syndrome (PCOS) is a common disorder affecting women in their reproductive age. Its prevalence differs according to ethnicity and diagnostic criteria, which ranges from 5.5% among Caucasians by using the 1990 National Institute of Health (NIH) criteria to 16% among women in the Middle East by using the 2003 Rotterdam criteria (1). PCOS is characterized by clinical or biochemical hyperandrogenism (such as hirsutism, acne, alopecia and seborrhoea) and ovulary dysfunction with or without polycystic ovaries (2). Notably, PCOS has been increasingly recognized as a complex illness that affects not only the medical aspects (such as insulin resistance, cardiovascular disease and endometrial cancer), but also the psychosocial aspects related to changes in physical appearance (3, 4). Apart from emotional disturbances, other important aspects of psychological well-being namely the sexual function and satisfaction in women with PCOS are often overlooked (5, 6).

Female sexual dysfunction (FSD) is very common with a prevalence of 21-28% among pre-menopausal women (7). It is defined as persistent or recurrent problems with sexual response, desire, orgasm or pain, which can have adverse effects on quality of life and inter-personal relationship (8). The Sexual Function Health Council of the American Foundation for Urologic Disease (AFUD) classified FSD into five main categories namely hypoactive sexual desire disorder, sexual aversion disorder, sexual arousal disorder, orgasmic disorder and sexual pain disorders (9). The risk factors of FSD include local genitourinary abnormalities (such as pelvic organ prolapse and urinary incontinence), ageing and hormonal and psychogenic disturbances (9, 10).

In women with PCOS, androgen excess and psychosocial changes may affect their sexual functions, although existing data are limited for drawing definitive conclusions (11). In the present meta-analysis, we compared the prevalence and severity of sexual dysfunction in women with and without PCOS. The primary outcome of this study was the prevalence of sexual dysfunction in women with PCOS compared to those without. The secondary outcome was the total and sub-scale scores of Female Sexual Function Index among women with PCOS and those without.

## **Methods**

#### Data sources and extraction

We performed a systematic search of all English-language medical literature published from inception till May 2018 from PubMed, CINAHL and Medline using the following Medical Subject Headings: "sexual dysfunction", "polycystic ovary", "polycystic ovary syndrome" and "polycystic ovarian syndrome". We also looked into references of the selected articles. When the articles were not available or information of the study cohort was inadequate, we attempted to contact the respective authors via e-mail to obtain the full articles and detailed data. Two independent reviewers (HHL and HSL) screened the titles and abstracts obtained through the electronic search and analysed the full-text articles. All duplicates were removed. Wherever data were not provided numerically, they would be read off graphs. Data from eligible studies were extracted by HHL and all extracted data were reviewed by AY and SK.

Structured interviews and self-reported questionnaires such as the Female Sexual Function Index (FSFI) and Changes in Sexual Functioning Questionnaire (CSFQ), have been widely used to assess FSD. FSFI is a validated 19-item self-report scale that evaluates sexual function of women within a 4-week window, based on six subscales namely sexual desire, arousal, lubrication, orgasm, satisfaction and degree of pain. The maximum score of each subscale is 6 and the maximum total score is 36. A score of <26 defines FSD (12).

#### Quality assessment

HHL and AY independently assessed the quality of the methodology and reporting of all studies using the Newcastle-Ottawa Scoring (NOS) Scale for Case-Control Studies or the NOS Scale adapted for Cross-Sectional Studies, as appropriate. Any discrepancies were discussed with the third reviewer (LLL). The NOS scale was developed to assess the quality of non-randomized case-control studies for the interpretation of meta-analysis results. Based on a "Star-graded" system, each study is assessed in three broad categories namely the group selection, group comparability and ascertainment of the outcome of interest (Exposure). In the original NOS Scale for Case-Control Studies, each study can be awarded a maximum of one star for every numbered item (four in the "Selection" category and three in the "Exposure" category) and a maximum of two stars in the "Comparability" category. In the NOS Scale adapted for cross-sectional studies, each study can be awarded a maximum of five stars in the "Selection" category, two stars for the "Comparability" category and three stars for the "Outcome" category. Both scales have a maximum score of 10.

#### Statistical analysis

#### Qualitative

All abstracted information was tabulated. A qualitative meta-analysis was conducted to summarize, compare and contrast the abstracted data.

#### Quantitative

All data analyses were performed using Stats Direct (version 2.7.9). The presence of heterogeneity between the trials was tested using the I-squared (I) statistic. An I of more than 40% indicated significant heterogeneity. If the I was significant, we pooled the data by using random-effects (DerSimonian-Laird). Conversely, we pooled the data by using fixed-effects (Mantel-Haenszel, Rothman Boice). We also assessed publication bias with Begg-Mazumdar and Egger test. For dichotomous outcomes, we estimated the relative risk (RR) with 95% confidence intervals (CI) using the random-effects model. For continuous outcomes, we estimated the weighted mean difference in FSFI score with 95% confidence interval (CI) if the mean and standard deviation (SD) of the outcomes were presented in the original articles.

## **Results**

The initial search identified a total of 2135 articles: 288 from PubMed, 324 from CINAHL and 1523 from MEDLINE. After the screening of titles and abstracts, removal of duplicate publications and screening of full-texts, we included 21 full-text articles in the present systematic review and meta-analysis (Figure 1).

A total of 5366 women with PCOS from 21 studies were included. The sample size ranged from 16 to 1594. There were 14 case-control studies, of which 13 were cross-sectional (5, 6, 13-23) and one prospective. (24) The remaining seven were cross-sectional single cohort studies. (25-31)

Table 1 described the study characteristics. All included studies evaluated FSD among women with PCOS, albeit using different scoring scales. Most studies used FSFI. Other sexual function scales used were Visual Analogue Score of sexual satisfaction (13), Index of Sexual Satisfaction (14), Italian McCoy Female Questionnaire (15, 16, 20), CSFQ (17), Arizona Sexual Experience Scale (25), Maudsley Marital Questionnaire (21) and the Polish version of Mell-Krat Scale (SFK/K scale) (23). The assessment method, rating, score range and interpretation of these scorings are listed in the Supplementary table. A total of 16 studies reported the proportion of women with PCOS and coexistent FSD (5, 6, 14-19, 24-31). Compared to women without PCOS, those with PCOS were younger (mean $\pm$ SD: age 28.90 $\pm$ 3.11 versus 31.42 $\pm$ 3.37 years; p<0.0001) and had higher body mass index (BMI; 27.76 $\pm$ 3.79 versus 24.95 $\pm$ 3.71 kg/m²; p=0.002), Ferriman-Gallwey score (9.90 $\pm$ 3.37 versus 4.11 $\pm$ 2.17; p<0.0001) and serum total testosterone level (2.26 $\pm$ 0.59 versus 1.51 $\pm$ 0.49 nmol/L; p<0.0001).

There was no significant difference in mean total FSFI score (25.72±2.33 versus 26.62±3.38; p=0.608) in women with and without PCOS (Figure 2A). For the FSFI subscales, women with PCOS had a lower score for the pain subscale than women without PCOS (4.60±0.71 versus 5.24±0.39; p<0.001) (Figure 2B). Other subscales were not significantly different between the two groups (Figures 2C-2G). In the fixed-effects model, women with PCOS had a 1.39 higher odds (95% CI 1.13, 1.72; p=0.002, p 11.9%) of having FSD than women without PCOS (Figure 3).

## **Discussion**

In the present meta-analysis of 21 observational studies, we have shown that women younger than 30 years with PCOS are 40% more likely to have FSD than women without PCOS. One-third of women with PCOS have FSD, suggesting that this coexistence is more common than expected and should not be overlooked in routine clinical practice. Although our findings of an increased likelihood of dyspareunia were different from another meta-analysis of 18 studies which showed decreases in the arousal, orgasm and satisfaction subscales, both had consistently demonstrated an excess risk of FSD in women with PCOS (32). Given the adverse impact on sexual satisfaction and quality of life, our results have indicated the need for a greater understanding of FSD in women with PCOS in order to identify new treatment strategies for improved care.

To date, the exact mechanisms of FSD in PCOS are not entirely clear, although changes in the sex hormones and psychosocial well-being have been hypothesised (11, 33). Menstrual irregularities and subfertility could have led to low self-esteem and emotional distress such as depression and anxiety that might impair sexual function and interpersonal relationships with their partners. (33-37) In addition, women with PCOS might find themselves less attractive due to body dissatisfaction and potential loss of feminine identity as a consequence of obesity and androgen excess (38). In a case-control study involving 200 Italian premenopausal women, 45% of women with metabolic syndrome had FSD, compared to only 23% in age- and body-weight matched controls (39). On the other hand, androgen excess was associated with high levels of miRNA-21, miRNA-27, miRNA-103 and miRNA-155 that might influence the expression of several genes responsible for hormonal cellular and sexual reproduction processes in PCOS and thus, an increased risk of FSD (40).

PCOS is characterized by high levels of androgens (dehydroepiandrosterone, androstenedione and testosterone), luteinising hormone (LH) and increased LH/follicle stimulating hormone (FSH) ratio (41). While androgen deficiency is linked to reduced sexual drive (42, 43), data in women with PCOS are limited with conflicting results (11, 33, 44). Nevertheless, our findings were similar to a Brazilian study involving 88 women with PCOS (mean age 27 years), which showed a positive association of either androgen excess or an elevated LH level with FSD (45). Notably, PCOS arises from a vicious cycle of androgen excess which promotes insulin resistance and compensatory hyperinsulinemia, as well as an amplification of LH-stimulated androgen secretion by the ovarian theca cells and adrenal glands, that can worsen sexual function (2). In addition, due to the androgen-induced insensitivity of hypothalamic gonadotrophin (GnRH) pulse generator to suppression by estrogen and progesterone (46), there is a

persistent and rapid GnRH pulsatility with preferential synthesis and release of LH over FSH, in which FSH is physiologically regulated by a slow GnRH pulse frequency (47). The relatively low FSH level prevents ovarian follicular growth, resulting in estrogen deficiency with possible vaginal atrophy. This may explain the increased risk of FSD, particular dyspareunia, as reported in the present analysis (2, 33).

There is a paucity of data on the treatment effects of PCOS on FSD (11). In an open-label, observational study of 64 women with PCOS (mean age 29.3 years), six months of metformin treatment reduced dyspareunia and improved sexual satisfaction and frequency of sexual intercourse, presumably due to improved insulin resistance (48). Another observational study involving 72 women with androgen excess (mean age 24.3 years) treated with anti-androgenic oral contraceptive pills (OCP), reported significant improvement in hirsutism, sexual pain, orgasm and satisfaction as early as 6<sup>th</sup> cycle and sustained till 9<sup>th</sup> cycle of OCP administration (49). Further research with a larger sample size is required to validate these interesting findings.

Our results can be generalised to a number of populations given that the pooled cohort involved women from North and South America, Europe, Middle East and Asia, we can generalise our results to a number of populations. Despite this diversity, the pooled analysis was of low heterogeneity as evidenced by the  $\ell$  statistic. Our study has several limitations. First, all included studies used self-reported questionnaires which could be subjected to information bias. Second, given all studies were observational in design, we were unable to provide the causal inference. Last, we were unable to evaluate the intervention effect on FSD due to a limited number of studies.

## Conclusion

In conclusion, FSD, particularly dyspareunia, is a prevalent and disabling condition in young women with PCOS. Sensitive probing into the intimate aspects of their sex lives is needed to further understand the struggles that afflict women with PCOS. While more resources are to be directed toward the screening of FSD in these women, parallel efforts should be undertaken to investigate the impact of new treatment strategies.

## **List Of Abbreviations**

PCOS Polycystic ovarian syndrome

FSD Female Sexual Dysfunction

NOS Newcastle-Ottawa Scale

FSFI Female Sexual Function Index

## **Declarations**

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The author(s) declared that they have no competing interests.

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Authors' contributions

HHL, HSL and AY performed systematic search and data extraction. HHL, AY and LLL assessed quality of methodology. AY and SK analysed the data. HHL, SK, BF and LLL drafted the manuscript. All authors read and approved the final manuscript.

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Not applicable

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## Figure 3

Figure 3, Proportion of female sexual dysfunction, was not included with this version of the manuscript

## **Figures**

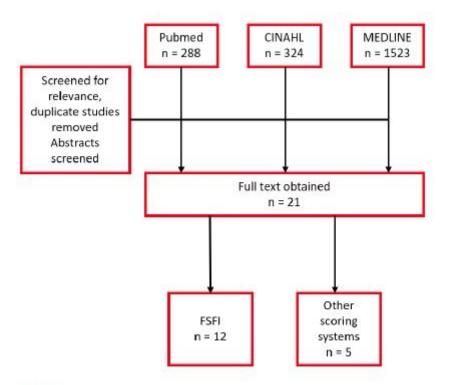
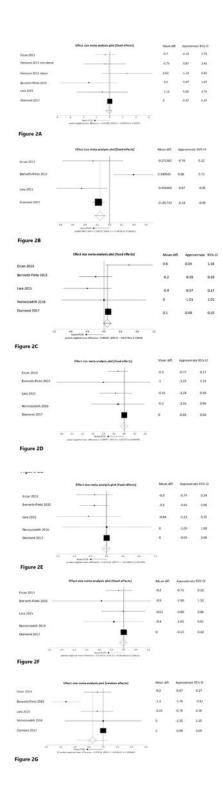


Figure 1

## Figure 1

Search Strategy



## Figure 2

A Total score of Female Sexual Function Index. B Pain subscale of Female Sexual Function Index. C Desire subscale of Female Sexual Function Index. D Lubrication subscale of Female Sexual Function Index. E Arousal subscale of Female Sexual Function Index. F Orgasm subscale of Female Sexual Function Index. G Satisfaction subscale of Female Sexual Function Index.

## **Supplementary Files**

This is a list of supplementary files associated with this preprint. Click to download.

- Supptablequestionnaire.pdf
- PRISMAchecklist.pdf
- Table1Studycharacteristics.pdf