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The Impact of Metabolic Syndrome and Its Components on Female Sexual Dysfunction: A Narrative Mini-Review

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Key Words
Metabolic syndrome • Female sexual dysfunction • Obesity • Systemic arterial hypertension • Diabetes mellitus • Dyslipidemia •

Abstract
Background: The impact of metabolic syndrome on female sexual dysfunction received modest consideration in clinical practice. The aim of the research was to analyze the international literature to determine the relationship between the metabolic syndrome, its components and female sexual disorders. ***Methods***: We identified relevant full-length papers by electronic databases as Index Medicus/Medline, Scopus, Life Science Journals, from 2005 to the present. Studies were searched using the following as search query: metabolic syndrome, female sexual dysfunction, obesity, systemic arterial hypertension, diabetes mellitus, dyslipidemia. ***Results:*** Women with metabolic syndrome showed higher prevalence of sexual inactivity and low sexual desire, orgasm and satisfaction respect to women without metabolic syndrome. Particularly metabolic components as diabetes mellitus, dyslipidemia, systemic arterial hypertension were strongly associated with lower sexual desire, activity and Female Sexual Function Index total score. In contrast, other studies showed no relationship. ***Conclusion:*** Our study showed that in the clinical evaluation of women with metabolic syndrome routine inquiring about female sexual dysfunction should be recommended to ameliorate sexual function and quality of life. However more prospective and longitudinal studies on the sexual effects of metabolic syndrome should also be suggested to know the factors related to women's sexuality better.

Introduction

Female sexual dysfunction (FSD) is a complex and growing health problem. However the result is often underestimated. A large international clinical study showed that 39% of sexually active women presented at least one sexual disorder [1] and, especially in postmenopausal women, this prevalence ranges between 25 and 79% [2–4].

FSD was defined as the difficulty in sexual response cycle as genital arousal disorder, female orgasmic disorder, hypoactive sexual desire, causing negative impact on quality of life and personal relationships [5–7].

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Table 1. Clinical studies evaluating the association between MS and FSD

Study design	Population	Assessment of sexual activity	Main results
The Rancho Bernardo study [25]	376 postmenopausal women	FSFI	MS was associated with low sexual activity, desire, arousal, orgasm and satisfaction
Observational, cross-sectional study [26]	111 postmenopausal women	FSFI	no relationship between MS and FSD
Cross-sectional cohort study [27]	256 menopausal women	–	no relationship between MS and FSD in menopausal women
Case-control study [28]	204 premenopausal women	FSFI FSDS MHQ	MS was associated with a higher prevalence of FSD, lower desire, arousal, lubrication and orgasm compared with controls. A significant correlation between increasing number of MS component and FSD was found
Case-control study [29]	195 postmenopausal women	FSFI	MS was associated in postmenopausal women with a higher prevalence of FSD, lower desire, arousal, lubrication, orgasm and satisfaction
Case-control study [2]	208 postmenopausal women	FSFI FSDS MHQ	MS was associated in postmenopausal women with a higher prevalence of FSD, an increased risk of lower lubrication, satisfaction arousal, orgasm
Cross-sectional study [30]	773 women	FSFI	no relationship between MS and FSD in middle- to old-aged women
Cohort study [31]	538 pre- and post-menopausal women	23-item FSD questionnaire	MS was associated only in premenopausal women with an increased risk of FSD, particularly reduced sexual desire
Case-control study [32]	200 premenopausal women	FSFI	MS was associated in premenopausal women with a higher prevalence of lower scores on the FSFI, predominantly in the sexual satisfaction

FSDS = Female sexual distress scale; FSFI = female sexual function index; MHQ = middlesex hospital questionnaire.

Sexual dysfunctions related to metabolic alterations receive modest consideration and limited research in clinical practice, especially in women, but their evaluation could reveal serious cardiovascular diseases, such as cerebrovascular diseases, coronary artery disease and peripheral arterial vascular disease, with increased morbidity and mortality, mostly in menopausal women [8, 9].

Several definitions of metabolic syndrome (MS) have been proposed and have been changing since 1998, including the World Health Organization; the National Cholesterol Education Program's Adult Treatment Panel III Report; the American Heart Association and the National Heart, Lung and Blood Institutes; and the International Diabetes Federation [10–13]. Overall in the varying accepted definitions, MS was defined by a cluster of medical comorbidities, including central obesity, insulin resistance, impaired glucose metabolism, dyslipidemia (hypertriglyceridemia, low high-density lipoprotein cholesterol), and systemic arterial hypertension [14]. MS and its components were related to increased risk of several pathological conditions as diabetes mellitus, cardiovascular diseases, polycystic ovarian syndrome, obstructive sleep apnea, fatty liver disease, cancer, primary antiphospholipid syndrome and other rheumatic diseases as systemic lupus erythematosus, rheumatoid arthritis, systemic sclerosis and fibromyalgia [15–24].

The aim of the research was to analyze the international literature to determine the relationship between the MS, its components and female sexual disorders.

Materials and Methods

Identification of Studies

We identified relevant full-length papers by electronic databases as Index Medicus/Medline, Scopus, Life Science Journals, from 2005 to the present.

Studies were found using the following key words: female sexual dysfunction, metabolic syndrome, obesity, systemic arterial hypertension, diabetes mellitus, and dyslipidemia. Supplementary papers were searched by reference of relevant papers screened for significant dates. Two independent scientists reviewed the articles in detail to examine only articles that analyze critically the relationship between MS and FSD.

Inclusion Criteria

Working independently, reviewers evaluated all eligible studies in full text. To be included articles had to (1) evaluate the association between MS and FSD; (2) contain an original data analysis and (3) from a peer-reviewed journal. Articles were excluded if the clinical study (1) presented only as a case report or had in-

appropriate design; (2) did not analyze a reciprocal relationship between MS and FSD or MS components and FSD.

Data Extraction and Quality Assessment

For each study were examined: study design, demographic characteristics, sample size, quality of study, outcomes relating to assessment of sexual activity and MS. Copies of all selected and included articles were found and archived for lecture in full. Due to significant heterogeneity of clinical studies we not pooled the data in a meta-analysis, but in a tabular summary. Results were reported in the following categories: (1) MS and FSD; (2) systemic arterial hypertension and FSD; (3) obesity and FSD; (4) dyslipidemia and FSD; (5) diabetes mellitus and FSD.

Results

Description of Studies

Total 35 studies met the inclusion criteria (table 1, 2) [2, 25–58]. Sixteen studies were classified as case-control studies [2, 28, 29, 32, 37–39, 41, 42, 44, 47, 49, 51, 52, 54, 57] and the rest as observational/cross-sectional studies. The number of participants ranged from 88 to 2,270 women. Only 9 studies looked specifically at MS [2, 25–32]. The remaining included data about components of MS [2, 33–58].

Women with MS showed higher prevalence of sexual inactivity and low sexual desire, orgasm and satisfaction respect to women without MS. Particularly metabolic components as diabetes mellitus, dyslipidemia, systemic arterial hypertension and obesity were strongly associated with lower sexual desire, activity and Female Sexual Function Index total score in pre- and post-menopausal women.

Principally women with systemic arterial hypertension presented a greater rate of FSD, evaluated by the Female Sexual Function Index questionnaire, versus normotensive women (90 and 41% respectively) and the use of antihypertensive medications was significantly related to lower prevalence of FSD [2, 25, 34, 35, 37].

Furthermore, in sexual active women FSD prevalence was greater in female with dyslipidemia, particularly hyperlipidemia and low high-density lipoprotein cholesterol, compared to normolipidemic women, independently from menopausal status and with direct relationship with cardiovascular disease [2, 41, 42].

Similarly diabetes mellitus and diabetes medications were associated with FSD, specifically lubrication and orgasm disorders, induced by vascular changes in the pelvis and neuropathic alterations in genital arousal, directly related to glycemic control and duration of diabetes [43–53].

It's possible also that diabetes mellitus caused a greater risk of vaginal infections, particularly recurrent Candidiasis, responsible of increased risk for dyspareunia.

In contrast, other studies showed no relationship between MS and FSD or metabolic components, particularly obesity, especially in postmenopausal women [26, 27, 30, 39, 40, 54].

Discussion

Female sexual function showed a combination of endocrine, vascular and neuromuscular factors that regulate important steps of female sexual reaction as increased genital blood flow, enlarged clitoral diameter and length, increased vaginal luminal diameter and lubrication, wall engorgement [59, 60].

Pelvic vascular injury and neuropathy induced by some metabolic factors as dyslipidemia, glucose intolerance, insulin resistance, diabetes mellitus, and systemic arterial hypertension could cause clitoral insufficiency and reduced vaginal engorgement resulting in vasculogenic FSD [37, 59–63]. In particular obesity, as the result of excessive accumulation of body fat, is strongly associated with MS. The development of fat cells (i.e. adipocytes) is known as adipogenesis. The adipogenesis is a continuous process even in adult adipose tissue for the presence of preadipocytes that can proliferate and differentiate [64]. Adipose tissue is not a simple energy storage organ, but exerts important endocrine and immune functions; it provides a link between MS, inflammation, cardiovascular, immune disorders and cancer [65–69].

Therefore MS and its components may influence and associate with the female sexual function through the chronic vascular inflammation, oxidative stress and atherosclerosis, which also can impair the genital blood flow and the oxygen supply to the female pelvis, especially in severe MS, impairing some domains of the female sexuality [8, 26, 70].

Nevertheless some studies showed no relationship between MS and FSD or metabolic components, particularly obesity, especially in postmenopausal women.

In general, the statistical power and importance of results obtained from these studies evaluating the relationship between MS and FSD could be further discussed because the largest part included a small number of participants, include a short follow-up period, or show evident selection bias (e.g. only voluntary patients attended a screening clinic, menopausal women etc.) and confounding factors as behavioral, psychological (e.g.

Table 2. Clinical studies evaluating the association between MS components and FSD

Study design	MS components	Population	Assessment of sexual activity	Main results
Systolic blood pressure intervention trial (SPRINT) [33]	systemic arterial hypertension	635 postmenopausal women	FSFI	systemic arterial hypertension was not associated with FSD
Observational, prospective, cross-sectional descriptive study [34]	systemic arterial hypertension	157 postmenopausal women	FSFI	hypertension was related to sexual dysfunction
Cohort study [35]	systemic arterial hypertension	540 postmenopausal women	FSFI	significant association between systemic arterial hypertension and FSD
Cohort study [36]	systemic arterial hypertension	1,390 postmenopausal women	–	systemic arterial hypertension was not associated with FSD
Case-control study [37]	systemic arterial hypertension	417 pre- and post-menopausal women	FSFI	FSD was present in 42.1% of hypotensive women and 19.4% of normotensive women
Case-control study [38]	obesity	120 pre- and post-menopausal women	Iranian version of FSFI	obesity was related to female sexual dysfunction
Case-control study [39]	obesity	91 premenopausal women	FSFI	no significant relationship between obesity and FSD
Population-based study [40]	obesity	1,266 pre- and post-menopausal women	FSFI	no significant association between obesity and FSD
Case-control study [41]	dyslipidemia	466 pre- and post-menopausal women	FSFI FSDS MHQ	dyslipidemia was associated with FSD
Case-control study [2]	dyslipidemia	208 menopausal women	FSFI FSDS MHQ	hypertriglyceridemia was linked to FSD
Case-control study [42]	dyslipidemia	556 premenopausal women	FSFI	women with hyperlipidemia had lower arousal, orgasm, lubrication, and satisfaction
Cross-sectional study [43]	diabetes mellitus	236 premenopausal women	FSFI	FSD was present in both type 1 and type 2 diabetes mellitus
Case-control study [44]	type 2 diabetes mellitus	260 premenopausal women	FSFI	type 2 diabetes was associated with lower sexual desire, arousal, lubrication, orgasm, sexual satisfaction
Diabetes control and complications trial/epidemiology of diabetes interventions and complications study (DCCT/EDIC) [45]	type 1 diabetes mellitus	580 pre- and post-menopausal women	FSFI	type 1 diabetes with autonomic neuropathy was associated with FSD
Cross-sectional single-center study [46]	type 2 diabetes mellitus	93 pre- and post-menopausal women	FSFI	type 2 diabetes was associated with arousal, desire, lubrication, orgasm, satisfaction problems and pain during sexual intercourse
Case-control study [47]	type 1 diabetes mellitus	170 pre- and post-menopausal women	FSFI FSDS	type 1 diabetes was significantly associated with higher FSD frequency
Cross-sectional study [48]	type 2 diabetes mellitus	150 premenopausal women	FSFI	type 2 diabetes mellitus was significantly associated with reduced lubrication, sexual desire, arousal problems, dyspareunia, orgasmic dysfunction
Case-control study [49]	type 1 and type 2 diabetes mellitus	118 premenopausal women	FSFI	type 1, but not type 2 diabetes mellitus was associated with FSD, particularly lubrication, arousal, orgasm, dyspareunia
Cross-sectional study [50]	type 2 diabetes mellitus	110 pre- and post-menopausal women	FSFI	type 2 diabetes mellitus was significantly associated with FSD
Case-control study [51]	type 1 diabetes mellitus	200 premenopausal women	FSFI	diabetes mellitus was significantly associated with FSD
Case-control study [52]	type 2 diabetes mellitus	222 pre- and post-menopausal women	FSFI	type 2 diabetes mellitus was significantly associated with FSD
Cross-sectional study [53]	diabetes mellitus	2,270 pre- and post-menopausal women	FSFI	insulin-treated diabetes mellitus was associated to FSD, particularly reduced lubrication and orgasm
Case-control study [54]	type 1 diabetes mellitus	144 pre- and post-menopausal women	FSFI	no significant relationship between type 1 diabetes mellitus and FSD
Cross-section study [55]	diabetes mellitus	544 pre- and post-menopausal women	FSFI	diabetes Mellitus was associated with orgasmic dysfunctions
Cross-section study [56]	diabetes mellitus	1,291 pre- and post-menopausal women	BACH FSFI	type 1 diabetes mellitus was associated with greater pain with sexual intercourse. Type 2 diabetes was related to better orgasm scores and satisfaction

Study design	MS components	Population	Assessment of sexual activity	Main results
Case-control study [57]	diabetes mellitus	88 pre- and post-menopausal women	FSFI	significant relationship between type 1 diabetes mellitus and FSD
Prospective cohort study [58]	type 1 diabetes mellitus	652 pre- and post-menopausal women	FSFI	type 1 diabetes mellitus was associated with loss of libido, orgasm disorders, lubrication and arousal and pain

FSDS = Female sexual distress scale; FSFI = female sexual function index; MHQ = middlesex hospital questionnaire; BACH FSFI = Boston Area Community Health Survey Female Sexual Function Index.

depression, body image, relationship with a partner etc.) and social risk factors (e.g. low socioeconomic status).

Conclusion

Overall our study showed that in the clinical evaluation of women with MS and its components, routine inquiring about FSD should be recommended to ameliorate sexual function and quality of life index. However more prospective and longitudinal studies on the sexual effects of MS should also be suggested to evaluate the relationship between FSD, MS and its components and to better know the factors related to women's sexuality.

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