

MENOPAUSE

Hyperglycemia in postmenopausal women screened for the metabolic syndrome is associated to increased sexual complaintsPETER CHEDRAUI¹, FAUSTINO R. PÉREZ-LÓPEZ², JUAN E. BLÜMEL³,
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Abstract**Background.** Postmenopausal metabolic changes increase cardiovascular risk and impair quality of life (QoL). Despite this, few reports have addressed the association of these changes with female sexuality.**Objective.** To determine the association between the metabolic syndrome (METS), and its components, and female sexuality.**Methods.** Data of sexually active postmenopausal women who participated in a METS screening program who filled out the menopause-specific quality of life questionnaire (MENQOL) were assessed. Specifically the sexual domain of the MENQOL was analyzed in regard to mean total and item scores (decreased *libido*, vaginal dryness, and sexual avoidance). Criteria of the Third Adult Treatment Panel (ATP III) were used to identify women with the METS.**Results.** Two hundred six women fulfilled inclusion criteria. Mean age of participants was 54 ± 6.9 years (median: 54 years). Prevalence of the METS in this sexually active postmenopausal series was 39.8%. About 52.9% of them presented abdominal obesity, 35.4% hypertension, 55.8% high triglycerides, 17.5% hyperglycemia, and 59.7% decreased high density lipoprotein cholesterol (HDL-C). Women with the METS as compared with those without the syndrome displayed no significant differences in MENQOL sexual scorings (total or of its composing items). Equally there were also no score differences among those presenting any of the five components of the METS, except women with hyperglycemia who significantly displayed a higher total sexual domain score (5.6 ± 2.1 vs. 4.8 ± 2.3 , $p < 0.05$) in association to a higher mean score in the decreased *libido* item (6.0 ± 2.3 vs. 4.8 ± 2.6 , $p < 0.01$). After controlling for several confounding factors, logistic regression confirmed that women with hyperglycemia were significantly at higher risk for presenting decreased *libido* (higher item score, OR 2.4, CI 95%: 1.0–5.7, $p < 0.05$) and more impaired sexuality (higher total MENQOL sexual domain score: OR, 2.5, CI 95%: 1.1–5.4, $p < 0.05$).**Conclusion.** Despite the limitations of this study, as assessed with the MENQOL, hyperglycemia in postmenopausal women screened for the METS was associated to a negative impact in sexuality. More research is warranted in this regard.**Keywords:** Menopause, sexual complaints, quality of life, metabolic syndrome, hyperglycemia**Introduction**

Cardiovascular disease (CVD) is rare in women younger than 45 years, but those older than 55 are more likely than men to have it [1,2]. Indeed, after the menopause the prevalence of the metabolic syndrome (METS) or any of its components increases in relation to time since the menopause, sedentary and bad habits [3–5]. This situation not only increases cardiovascular risk [6] but also increases severe menopausal symptoms [7–9] and hence impairing quality of life (QoL) significantly. Elevated body mass

index (BMI) is associated with poor QoL during the climacteric [10–12]. The association between low testosterone levels and erectile dysfunction in men with the METS is receiving increasing attention. Indeed, men with the METS report a significantly higher proportion of moderate to severe erectile dysfunction [12]. Female sexual dysfunction (SD) is associated with different psychosocial, genital, and functional diseases. Recent data seem to point out the fact that premenopausal METS increases the risk of SD [13] and it may have an independent role through impairment of sexual desire [14]. Items composing

the METS such as elevated BMI and hypertension have also been independently associated with female SD [15,16]. Although pre- and postmenopausal women exhibit differences in sexual index [17], data regarding female SD and postmenopausal METS is scarce. In this sense, one study can be found in the literature that assessed urogenital symptoms by race/ethnicity in a large exclusively postmenopausal population ($n=98,705$) and determined that vaginal dryness, irritation or itching, discharge and dysuria were elevated among women who are Hispanic, obese, and/or diabetic [18].

The objective of the present research was to determine the association between the METS (and its components) and female sexuality, as assessed by the menopause-specific quality of life questionnaire (MENQOL).

Methods

Participants

From February 1, 2005 to March 31, 2005 a METS screening program aimed to determine the prevalence of this entity and related risk factors among postmenopausal women was carried out at the Institute of Biomedicine of the Universidad Católica of Guayaquil, Ecuador. In brief, a total of 325 women (>1 year amenorrhea), with intact uterus, aged ≥ 40 years, non-hormone therapy (HT) users participated in this program. Women were recruited through newspaper advertising and attended the program after an 8-hour overnight fasting period. Waist circumference, height, and blood pressure measurements were recorded as well as blood sampling was performed for the determination of serum glucose and lipid profile analysis. Basal characteristics of these participants ($n=325$) as well as the main results of this program are presented elsewhere [3]. As a secondary objective, QoL was also measured using a specific menopausal instrument, data which is also presented elsewhere [8]; however, data specifically regarding the sexual domain of the MENQOL and its composing items among those sexually active ($n=206$) were further explored, analyzed, and presented in this document. General data included: age, age at menopause presentation, time elapsed since menopause, residency, income, and habits (smoking, alcohol, and sedentarism).

Criteria of the Third Adult Treatment Panel (ATP III) were used to define those with METS, this is three or more of five risk determinants: abdominal obesity (waist circumference > 88 cm), increased serum triglycerides (≥ 150 mg/dl), decreased high density lipoprotein cholesterol (HDL-C < 50 mg/dl), high fasting glucose (≥ 110 mg/dl), and increased blood pressure ($\geq 130/85$ mmHg) [19]. BMI was

calculated as weight in kilograms divided by squared height in meters. Women with a BMI ≥ 30 were considered as obese.

Quality of life assessing tool

QoL was assessed using the MENQOL, proposed by Hilditch et al. [20], in its Spanish version [21]. The questionnaire is composed of 29 items grouped in four domains: vasomotor, psycho-social, physical, and sexual. Each item can be scored from 0 to 6 according to the intensity. No total MENQOL score is available, rather a mean total score within each domain (or of each of its composing items) can be generated according to each subject's response. The higher the scores within each domain, or in a particular item, the greater the impairment. Sexual domain of the MENQOL, specifically analyzed in this document, is composed of three items relating to sexual complaints: decreased *libido*, vaginal dryness, and sexual avoidance.

Statistical analysis

Data analysis was performed using EPI-INFO 2000 statistical software (Centers for Disease Control and Prevention, Atlanta, GA/World Health Organization, Geneva, Switzerland). Data are presented as means, medians, standard deviations, and percentages. Comparison of continuous data was performed with ANOVA. Logistic regression was used to analyze risk factors related to presenting higher scores in the MENQOL sexual domain (total and per item). Independent variables to be entered in the regression model were: age, age at menopause presentation, time elapsed since menopause, BMI, residency, income, habits (smoking, alcohol, and sedentarism), and the presence of the METS and each of its components separately. Continuous variables were converted into dichotomic values using medians as cut-off points. Entry of variables into the model was considered with a 20% significance level and the stepwise procedure performed. A p value of < 0.05 was considered as statistically significant.

Results

Data of a total of 206 postmenopausal sexually active women who had participated in the METS screening program were analyzed. Mean age was 54 ± 6.9 years (median: 54 years). About 48.5% had 5 or more years since menopause onset (occurring in average at 47.3 ± 4.8 years), 89.3% were mestizo, 91.7% were urban living and 48.5% were of low income. Regarding habits: 46.6% were sedentary and 2.9% were current smokers and/or abused alcohol.

Prevalence of METS in this sexually active postmenopausal series was 39.8%. About 52.9% of

them presented abdominal obesity, 37.5% had BMI ≥ 30 , 35.4% hypertension, 55.8% high triglycerides, 17.5% hyperglycemia, and 59.7% low HDL-C. No significant differences were found in socio-demographic characteristics between women with METS as compared with those without the syndrome.

Presented in Table I is the sexual domain of the MENQOL (mean total and per item scores) among the sexually active postmenopausal ($n = 206$) women who attended the screening program. No significant differences were found in mean total sexual domain score (5.1 ± 2.2 vs. 4.8 ± 2.4 , $p = \text{NS}$), decreased *libido* (5.2 ± 2.6 vs. 4.8 ± 2.6 , $p = \text{NS}$), vaginal dryness (5.1 ± 2.5 vs. 4.6 ± 2.8 , $p = \text{NS}$), or sexual avoidance (5.0 ± 2.7 vs. 5.0 ± 2.9 , $p = \text{NS}$) when METS women were compared with those without the syndrome. Equally there were also no differences in scorings among those presenting any of the five components of the METS, except for women with hyperglycemia who displayed significantly higher total sexual domain scores (5.6 ± 2.1 vs. 4.8 ± 2.3 , $p < 0.05$) in association to a higher mean score in the decreased *libido* MENQOL item (6.0 ± 2.3 vs. 4.8 ± 2.6 , $p < 0.01$).

After controlling for several confounding factors, logistic regression confirmed that women with hyperglycemia were significantly at higher risk for

presenting decreased *libido* (higher item scorings; OR: 2.4; CI 95%: 1.0–5.7, $p < 0.05$) and more impaired sexuality (higher total MENQOL sexual domain scores; OR: 2.5; CI 95%: 1.1–5.4, $p < 0.05$).

Discussion

The menopause transition is characterized by an increase in emotional lability, body weight, metabolic changes, urogenital discomfort, and sleeping disorders – among others – that alter daily life. It is also associated to bio-psycho and social difficulties, high rates of depressive symptoms, and female SD which have been associated to both, individual and partner factors [22–25]. Some changes are related to hormonal and metabolic changes and others rather due to familial and social adjustments [26–30]. Although there is no consensus regarding the definition of SD, its prevalence increases as men and women age; depending on the used diagnostic tool it has been reported that adult women (40–45%) and men (20–30%) have at least one manifestation of SD [29,31–33]. There are a number of common risk factors associated to female SD that include: individual general health status, genitourinary disease, psychiatric disorders, chronic diseases (i.e. diabetes, hypertension, cardiovascular), bad habits (i.e. smoking, alcohol), and socio-demographic

Table I. The sexual domain of the MENQOL (mean total and item score) in sexually active postmenopausal women attending the METS screening program ($n = 206$).

| Parameter | Sexual domain MENQOL | | | |
|--|------------------------|-----------------|------------------|------------------------|
| | Decrease <i>libido</i> | Vaginal dryness | Sexual avoidance | Total sexual score |
| All ($n = 206$) | $5.0 \pm 2.6^*$ | 4.8 ± 2.7 | 5 ± 2.8 | 4.9 ± 2.3 |
| Age ≥ 54 years (median) | | | | |
| Yes, 88 (42.7%) | 5.0 ± 2.7 | 5.0 ± 2.8 | 5.1 ± 2.8 | 5.0 ± 2.4 |
| No, 118 (57.3%) | 4.9 ± 2.6 | 4.6 ± 2.7 | 4.9 ± 2.7 | 4.8 ± 2.3 |
| Metabolic syndrome | | | | |
| Yes, 82 (39.8%) | 5.2 ± 2.6 | 5.1 ± 2.5 | 5.0 ± 2.7 | 5.1 ± 2.2 |
| No, 124 (60.2%) | 4.8 ± 2.6 | 4.6 ± 2.8 | 5.0 ± 2.9 | 4.8 ± 2.4 |
| Abdominal obesity | | | | |
| Yes, 109 (52.9%) | 5.0 ± 2.7 | 4.8 ± 2.8 | 5.1 ± 2.8 | 5.0 ± 2.4 |
| No, 97 (47.1%) | 4.9 ± 2.6 | 4.7 ± 2.7 | 5.0 ± 2.8 | 4.9 ± 2.3 |
| Obesity BMI ≥ 30 | | | | |
| Yes, 77 (37.4%) | 5.2 ± 2.8 | 4.8 ± 2.8 | 5.3 ± 2.8 | 5.0 ± 2.5 |
| No, 129 (62.6%) | 4.8 ± 2.5 | 4.8 ± 2.7 | 4.8 ± 2.7 | 4.9 ± 2.2 |
| Hyperglycemia (≥ 110 mg/dl) | | | | |
| Yes, 36 (17.5%) | 6.0 ± 2.3 | 5.3 ± 2.7 | 5.7 ± 2.6 | 5.6 ± 2.1 |
| No, 170 (82.5%) | $4.8 \pm 2.6^\ddagger$ | 4.7 ± 2.7 | 4.9 ± 2.8 | $4.8 \pm 2.3^\ddagger$ |
| Hypertension | | | | |
| Yes, 73 (35.4%) | 4.9 ± 2.7 | 4.7 ± 2.6 | 4.7 ± 2.7 | 4.8 ± 2.4 |
| No, 133 (64.6%) | 5.0 ± 2.6 | 4.9 ± 2.7 | 5.2 ± 2.8 | 5.0 ± 2.3 |
| High triglycerides (≥ 150 mg/dl) | | | | |
| Yes, 115 (55.8%) | 5.0 ± 2.6 | 4.7 ± 2.7 | 5.1 ± 2.7 | 5.0 ± 2.3 |
| No, 91 (44.2%) | 4.9 ± 2.6 | 4.9 ± 2.7 | 4.9 ± 2.9 | 4.9 ± 2.3 |
| Low HDL-C (< 50 mg/dl) | | | | |
| Yes, 123 (59.7%) | 4.8 ± 2.6 | 4.7 ± 2.6 | 4.8 ± 2.7 | 4.7 ± 2.3 |
| No, 83 (40.3%) | 5.3 ± 2.7 | 4.9 ± 2.9 | 5.4 ± 2.8 | 5.1 ± 2.4 |

*Mean \pm standard deviation; $^\ddagger p < 0.05$.

conditions [34]. Dennerstein et al. [35] recently reported the prospective assessment of an 11-year follow-up of mid-aged Australian women, showing that all domains of sexual function declined over the study period, in association to higher depressive scores and more negative feelings for their partners.

Various validated tools have been used to determine how the climacteric influences QoL [36], one even originally designed in Spanish [37]. In the present investigation the MENQOL tool, proposed by Hilditch et al. [20], was used which is based upon women's own perspective. This tool has been validated upon climacteric Hispanic populations and used to assess how the menopause impairs QoL [8,21]. Among Chilean women low sexual desire is the main reason for ceasing sexual activity. However, stopping sexual relationships do not seem to be important in marital stability [38]. Although SD risk among middle-aged Ecuadorian women [22,39] and within other Hispanic female populations [38,40,41], has been related to social, cultural, economic factors and to menopausal symptom severity, to the best of our knowledge however few or no study, addressing a postmenopausal Hispanic population, has determined the effect of the METS and its determinants over sexuality as assessed with the sexual domain of the MENQOL.

The prevalence of the METS increases during the fifth and sixth decade of women's life [3,42]. It is more frequent after the menopause onset, hence associated to, but not conclusively directly caused by the lower estrogenic milieu, that enhances several metabolic derangements (i.e. increased insulin resistance, obesity, hyperglycemia). Prevalence found in this postmenopausal series was high, however similar to rates recently found among several Latin American populations [42]. As assessed with the MENQOL tool we have previously reported that the METS impairs all QoL domains in postmenopausal women (vasomotor, psycho-social, physical and sexual) [8]. In the present document, we further explored the MENQOL sexual domain data in order to ascertain the impact of the METS and its components upon female sexuality. In one study, sexuality was assessed with the Female Sexual Function Index (FSFI) among premenopausal women with the METS and a matched control group [13]. The authors showed that women with the METS had an increased prevalence of SD as compared with the control group; upon individual analysis of the different domains it was found that women with the METS reported significantly lower arousal, orgasm, and lubrication scores in comparison to women without the METS. In a more recent paper [14], it has been reported that the METS was an independent risk factor for impaired sexual desire; however, this association was found among preme-

nopausal women. Contrary to this, the present study could be the first to report upon a postmenopausal series, in which hyperglycemia, a component of the METS, was related to a more impaired sexuality (higher decreased *libido* and total sexual domain scores). Hence, hyperglycemia could be a significant factor for presenting sexual complaints in the postmenopausal phase. It has been reported that type II diabetes has a negative impact on female sexual desire, orgasmic capacity, lubrication, sexual satisfaction, and the partner relationship [43]. Chronic hyperglycemia in the diabetes mellitus state is a major cause of serious micro- and macrovascular disease, affecting, therefore, nearly every corporal system. SD frequency is higher in diabetic men compared with healthy controls. Although diabetic complications are similar in both sexes, little attention has been given to the effects of diabetes on female sexuality and sexual function. Previous studies in women with diabetes may also neglect the importance of the subjective qualities associated with female sexuality and sexual domain. Both male and female diabetics had more arousal phase dysfunctions than did healthy spouses. In diabetic women, SD has been related to depression and to partner relationship quality. Logistic regression has demonstrated that in type I diabetic women, SD is related to psychological factors and depression [44,45]. It seems that diabetic women with SD did not differ from diabetic women without SD as for metabolic control, insulin dose, duration of diabetes, or frequency of diabetic complications [44]. Although depressive symptoms have been related to SD in women with diabetes, a recent postmenopausal series, using the FSFI tool and controlling for depression, determined that diabetes was an important and independent risk factor for SD [46].

On the other hand, it seems plausible that endothelial dysfunction in women with METS could have a negative effect on sexual response. However, we do not know if our results (increased sexual complaints) could be the expression of a primary step triggered by hyperglycemia equal to that found among diabetic women without vascular complications displaying oxidative stress marker alterations [47]. Men with SD show a lack of nitric oxide (NO) production and a significant increase in NO synthase binding sites in penile tissues, induced by diabetes [48]. These individuals also display expression of vascular damage mediators such as vascular endothelial growth factor (permeabilizing and neo-angiogenic effects) and endothelin-1 (vasoconstricting and mitogenic action). Neuropathy is also likely to be an important cause of diabetic erectile dysfunction [48,49]. Although we cannot ascertain whether these changes are present among the individuals of our series (with hyperglycemia and impaired sexuality), sexual impairment may be

representing an early clinical marker of the METS and related endothelial dysfunction. More research in this regard is needed to establish biochemical markers and pathways that could conclusively link sexual impairment in postmenopausal women with the METS or any of its components. In men, antioxidant treatment associated with sildenafil reduces activation and markers of endothelial damage [48]. In women this situation could be more complex especially among postmenopausal women who have steroid gonadal hormone deprivation. To make matter worse, it has been postulated that the interaction between testosterone and estradiol may determine the risk of developing the METS during the menopausal transition [50]. The female climacteric transition is a period of estrogenic deficiency and relative androgen excess as androgen synthesis is only mildly altered. Thus, postmenopausal women have a mild decrease in androgen production as compared with the premenopausal ones. Unfortunately, testosterone and/or sexual hormone binding globulin status were not assessed in our series that could give insights on the role of androgen deficit over sexual impairment. However, one must bear in mind that the METS would be a characteristic expression of climacteric hyperandrogenism predominance [4,51–54], situation that would contrarily not favor sexual impairment as found in the present series.

In any case, one must take into account that there are several cultural and lifestyle factors that change some sexual indices during the menopause [55], and also some differences in the prevalence of the METS and cardiovascular risk [56]. The existing evidence suggests that the promotion of healthy lifestyle practices by health care providers is a valuable strategy for reducing CVD risk in women transitioning through the menopause. The results of this series indicate that the promotion of these lifestyle changes (aimed in reducing adiposity and improving glucose control) should be equally encouraged; however the impact that such a program could have over sexual impairment in postmenopausal women with METS or its components remains to be determined. As the METS is very frequent in middle-aged women, its optimal management therefore would be expected to benefit their sexual sphere and relieve many non-specific complaints.

Finally, as for the limitation of the present study, one can mention its cross-sectional nature (i.e. small sample), the lack of serum androgenic level assessment among participants, and not being able to assess sexuality with a specific tool (i.e. the FSFI as compared to the MENQOL sexual domain that only has three items), all which do not allow drawing definitive conclusions; however, it adds to the few or null reports addressing, in a specific postmenopausal Hispanic population, the effect of the METS and its components over sexuality.

Despite the mentioned limitations, as assessed with the sexual domain of the MENQOL tool, the present series determined that hyperglycemia in postmenopausal women was associated to a negative impact in sexuality. More research is needed to further delineate pathogenic mechanisms involved in this regard.

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