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Original Research Article

Association of metabolic syndrome and lower urinary tract symptoms amongst South Indian postmenopausal women

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ABSTRACT

Background: Women spend one third of their life in menopause. The age related anatomical and physiological changes predispose them to MetS and lower urinary tract symptoms (LUTS). The aim was to study the prevalence of metabolic syndrome (MetS) and lower urinary tract symptoms in postmenopausal women attending menopause clinic, to study the correlation of LUTS and body composition among women with MetS.
Methods: 154 post-menopausal women who attended menopause clinic at the Christian Medical College Hospital Vellore, were recruited. MetS was diagnosed using IDF criteria. LUTS were assessed BFLUTS questionnaires. Blood was taken to assess serum fasting glucose and lipid profile. DEXA was performed to assess the whole-body composition.
Results: Of 154 postmenopausal women, 64% had MetS and 43% of women had a total LUTS score > 5. 90% of women had filling symptoms,57% had incontinence,17% had voiding symptoms,14 % had quality of life issues and 6 % had sexual symptoms. However, there was no statistical significant difference between two groups in correlating the variables of MetS with LUTS (P >0.05). The percentage of total body fat by DEXA scan was significantly greater (P=0.006) in women with MetS (37.32±5.04) when compared to the women without MetS (34.629±3.65).
Conclusions: Prevalence of MetS among the study population was 64 %. LUTS were observed in 43% of the patients. There was no significant difference in LUTS in women with MetS and without Mets. However, there was a significant difference in body composition among women with and without MetS.

Keywords: Body composition, DEXA scan, LUTS, Metabolic syndrome, Postmenopausal women

INTRODUCTION

Metabolic syndrome (MetS) is a global public health problem. Women spend nearly one third of their life in menopause. The hypoestrogenic milieu in menopausal women predispose them to develop MetS.[1] Women with MetS have a combination of metabolic abnormalities which include obesity, type 2 diabetes mellitus or impaired glucose tolerance, hypertension and dyslipidemia. These women are twice as likely to have heart attack or stroke and have a fivefold greater risk of developing type 1 diabetes.[2] The incidence of MetS in postmenopausal Indian women has been reported to be as high as 55%.[3] The age related anatomical and physiological changes predispose them to lower urinary tract symptoms (LUTS). The higher insulin level in women with MetS has been implicated in the development of LUTS. However, there is limited evidence currently available on the prevalence of MetS in

post-menopausal women and their association with LUTS. Hence, we designed a prospective study to assess the prevalence of MetS and their association of LUTS in postmenopausal women in relation to their body composition.

METHODS

This is a prospective cross sectional study performed in a tertiary care hospital in southern India. The study protocol was approved by the institutional research and ethics committee. A written informed consent was obtained from all the study participants. 154 postmenopausal women attending Menopause clinic were included. Women with thyroid disease, Cushing's disease, premature menopause, and surgical menopause, use of hormone therapy, chemotherapy, and radiotherapy were excluded.

Postmenopausal women were assessed for MetS based using International Diabetes Federation criteria IDF-2005.[4] As per these criteria, women with abdominal obesity defined as waist circumference ≥80cm in South Asians with any two of the four criteria's which included blood pressure ≥ 130/85 mmHg; fasting blood sugar level ≥ 100mg/dl; fasting serum triglyceride ≥150mg/dl; high-density lipoprotein cholesterol <50mg/dl were diagnosed to have MetS. Waist circumference was measured in erect position as the smallest horizontal girth between the costal margins and the iliac crests at minimal respiration using a fibre tape. Blood pressure was recorded in the right arm in sitting position. Venous blood samples were collected after an overnight fasting to measure serum total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, fasting plasma glucose and serum insulin.

Lower urinary tract symptoms were evaluated using Bristol Female Lower Urinary Tract Symptoms Index Scored Form.[5] The BF-LUTS score quantifies symptoms of incontinence along with their impact on sexual function and quality of life that are not commonly included in other female questionnaires. It includes variables like incontinence (I -5 items); voiding (V-3 items); and filling (F-4 items); with additional subscales for sexual function (S-2 items) and quality of life issue (QoL-5 items). Filling symptoms includes nocturia (F1), urgency (F2), dysuria (F3) and daytime frequency (F4) scaled between 0-4 (never- all the time). Voiding symptoms includes hesitancy (V1), straining (V2) and poor stream (V3) scored as 0-4. Incontinence symptoms include urge incontinence (I1), number of leaks per day (I2), stress incontinence (I3), Idiopathic incontinence(I4) and Nocturnal incontinence(I5) scored as above. Sexual symptoms were assessed as sexual dysfunction (S1) and coital incontinence (S2). Quality of life was assessed using four questionnaire which includes using protection (QoL1), fluid restriction (QoL2), affecting social life (QoL3) and overall quality of life (QoL4). Based on the median LUTS score of >5 in this study, we decided to take cut off of BF-LUTS score of 5 to study the prevalence of LUTS. The body fat composition was measured using Hologic dual energy X-Ray absorptiometry (DEXA) QDR 4500. Adipose tissue indices have been measured using the following variables Total Body fat %, Fat Mass/Height^2 (kg/m^2), Android / Gynoid ratio, %Fat Trunk/% Fat Legs, Trunk / Limb Fat Mass ratio, estimated visceral adipose tissue Mass (g), estimated visceral adipose tissue volume (cm^3), estimated visceral adipose tissue area (cm^2), Lean / Height (Kg/m^2) and Appen. Lean/ Height^2 (Kg/m^2).

Statistical analysis

The data was analyzed using SPSS (version 16.0; Chicago, IL, USA). All the data were presented as mean and standard deviations. The sample size was calculated on the basis of the expected prevalence of MetS. The reported prevalence of MetS for postmenopausal women was 41%. The clinical variables including patient's age, year of menopause, blood pressure, height and weight. The laboratory characteristics including fasting lipid profile, fasting plasma glucose, and score of menopause rating scale between the MetS and non-MetS groups were compared using Student's t test. The relationship between MetS and lower urinary tract symptoms were evaluated by the Chi-square test and analysis of covariance (ANCOVA). The relationship between the risk factors of MetS and LUTS score was determined by a linear regression test and the Kruskal–Wallis test. A p value of <0.05 was considered to be statistically significant.

RESULTS

In this study, 64% of women had MetS (n=99). Nearly One-third of women (n=32) were diagnosed to have MetS within 5 years of attaining menopause. The prevalence was found to increase with the years since menopause. 27% of women had MetS within 5-10 years of menopause whereas more than 40% of women were found to have MetS >10 years since menopause. Metabolic syndrome doubled in women with menopausal age more than 5 years.(n=67) (Figure 1).

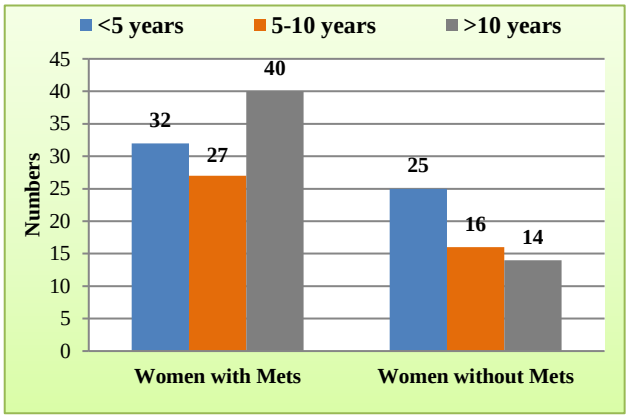

Figure 1: Women with and without metabolic syndrome.

Table 1: Demographic characteristics.

Demographic data	Women with Mets (Mean±SD) n=99 (64%)	Women without MetS (Mean±SD) n=55 (36%)	P-value
Age (years)	58.22±7.2	57.60±5.60	0.659
Years since menopause (years)	10.10±6.7	8.85±7.29	0.300
Menopausal age (years)	48.13±4.9	48.74±5.38	0.490
Height (cm)	152.99±5.27	152.00±6.60	0.342
Weight (kg)	65.77±11.52	59.76±16.64	0.020
BMI (kg/m^2)	28.19±5.38	25.84±6.89	0.031

There was no statistical significant difference between two groups in terms of age, menopausal age, the number of years since they attained menopause. However patients with MetS weighed heavier than women with MetS (P=0.02), thereby greater body mass index than the patients without MetS (P=0.031) (Table 1). Prevalence of total LUTS score >5 among postmenopausal women in our study group was 43%. 90% of women had filling symptoms, 57% had incontinence, 17% had voiding symptoms, 14% had quality of life issues and 6% had sexual symptoms.

Table 2: LUTS with metabolic syndrome.

Variables	Presences of symptoms in both groups	MetS Present n = 99	MetS Absent n = 55	P value
Filling	90.9%	66.4%	33.6%	0.079
Voiding	17.5%	55.6%	44.4%	0.297
Incontinence	57.1%	67.0%	33.0%	0.409
Sexual	6.5%	60.0%	40.0%	0.770
QOL	14.4%	60.0%	40.0%	0.129

LUTS: Lower Urinary Tract Symptoms; QOL: Quality of Life

However, postmenopausal women with MetS had total LUTS score of 62% with 66.4% having filling symptoms, 55.6% with voiding symptoms, 67% with urinary incontinence, 60% with sexual symptoms and 60% with poor quality of life. Women without metabolic syndrome had total LUTS score of 38%. However, there was no statistical significant difference between two groups (Table 2).

Table 3: Correlation of variables of metabolic syndrome with LUTS.

Variables	Flow	Voiding	Incontinence	Sexual symptoms	Quality of life
Hypertension	92.3 %	14.1 %	57.7%	9%	17.9%
Dyslipidemia	91.3 %	15.7 %	56.7%	7.1%	15%
Diabetes mellitus	91.3 %	15.2 %	58.7%	5.4%	15.2%
Waist circumference	92 %	15.2 %	57.7%	5.8%	16.8%
BMI	93 %	17.5 %	59.5%	5.4%	12.6%

Table 4: Adipose indices of body composition analysis using DEXA scan.

Variables	Women with MetS	Women without MetS	P value
Total Body % Fat	37.326±5.0477	34.629±3.6581	0.006
Fat Mass / Height^2 (kg/m^2)	10.520±3.2032	11.925±17.8086	0.682
Android / Gynoid ratio	0.963±0.1121	0.910±0.1344	0.079
%Fat Trunk / % Fat Legs	0.8133±0.16541	0.8075±0.12198)	0.854
Trunk / Limb Fat Mass ratio	0.9271±0.16244	0.8618±0.18605	0.116
Est.VAT Mass (g)	5.0477E2±200.74557	4.2036E2±158.98572	0.036
Est.VAT Volume (cm^3)	5.4572E2±216.99369	4.5436E2±171.86821	0.036
Est.VAT Area (cm^2)	106.49±39.465	87.18±32.937	0.019
Lean / Height (Kg/m^2)	16.381±2.2264	15.321±2.3459	0.049
Appen. Lean/Height^2 (Kg/m^2)	6.6505±98521	6.3232±0.90825	0.129
Lean / Height (Kg/m^2)	16.381±2.2264	15.321±2.3459	0.049

The filling symptoms were found to be the predominant symptom in women with MetS. Urinary incontinence was found in more than half of the women with metabolic syndrome However, there was no statistical significant difference between two groups in correlating the variables of metabolic syndrome with lower urinary tract symptoms (P >0.05) (Table 3).

The percentage of total body fat by DEXA scan was significantly greater (P=0.006) in women with MetS (37.32±5.04) when compared to the women without MetS (34.629±3.65). Similarly, the estimated visceral adipose tissue mass, volume and area were significantly higher in women with MetS when compared to the women without MetS (P<0.05) There was no difference in android and Gynoid ratio, percentage of fat in trunk to leg, trunk to

limb fat mass between two groups (Table 4). The lean mass index, the ratio of Lean / Height (Kg/m^2) is greater (P=0.049) in women with MetS (16.3 kg/m^2) compared to women without MetS (15.3 kg/m^2). However, there was no difference in the appendicular lean mass index between two groups (P=0.129).

DISCUSSION

Women with MetS is associated with double the risk of death, triple the risk of developing myocardial infarction or stroke compared to those without MetS.[6]

The prevalence of MetS varies with different diagnostic criteria. In this study, we found the prevalence of MetS using IDF criteria was 64%. Heidari et al described the prevalence of MetS was 44.9%, 57.9% and 64.3% in premenopausal, perimenopausal and postmenopausal women respectively which was comparable to this results.[7] In a study by Figueiredo et al, the prevalence of MetS using IDF criteria was 64.5% which was comparable to this study.[8] However, the same criteria used by Pandey and colleagues documented the prevalence of 55% in Western India.[9] A meta-analysis by Mendes and colleagues described a higher prevalence of MetS during the postmenopausal phase than the premenopausal, regardless of population.[10]

Menopause is marked by changes in body fat distribution, especially accumulation of visceral fat, rather than subcutaneous fat. The low skeletal mass and high fat mass in post-menopausal women may have a synergistic effect on both physical disability and metabolic impairment.[11]

To date, numerous evidences are available correlating LUTS in men with MetS. However, the prevalence of female LUTS in post-menopausal women with MetS have been underestimated. LUTS have significant negative impact on quality of life. Women with Mets have inflammatory sympathetic over activity, pro-inflammatory status, oxidative stress and endothelial dysfunction which predispose them for LUTS. Insulin resistance in MetS was a key component in the origin of LUTS. The loss of autonomic neurons with sympathetic over activity predispose them to develop voiding symptoms and decrease in bladder contractility.[12] Similarly, the decreased perfusion of the bladder and its neck leads to bladder ischemia, thereby loss of smooth muscle wall causing LUTS.[13]

BF-LUTS score more than 5 was seen in 43 % of the postmenopausal women. There was no significant correlation between MetS components and variable domains in the BF-LUTS score. There was no significant difference in Total LUTS and individual components in patients with respect to BMI. It is consistent with the study by Temml et al where the authors reported that the proportion of LUTS and the mean International Prostate Symptom Score (IPSS) did not significantly differ with the presence or absence of MetS in people of either gender.[14] In a study regarding relationship between female sexual dysfunction and MetS, Ponholzer et al reported that in a total of 538 women with a mean age of 44 years, MetS was an independent risk factor for impaired sexual desire (p = 0.03) with an age-adjusted OR of 3.3 (95% CI, 1.5–7.3).[15] Esposito and Giugliano showed that premenopausal women with MetS had a reduced mean full Female Sexual Function Index score (p=0.001).[16] However In this study, there was no significant difference between two groups which could be attributed to the socio-cultural differences and attitude toward menopause.

In this study, filling symptoms were found to be greater than voiding symptoms in women with MetS. However, Kuplien and colleagues described that women with MetS had greater voiding symptoms over fillings symptoms.[17] In a survey involving 2911 postmenopausal women by Wennberg et al documented predominant storage symptoms when compared to filling or incontinence.[18] These authors concluded that better awareness among postmenopausal women along with easy access to health care significantly reduced LUTS. Tai et al analysed the effect of MetS components on LUTS in their study involving 850 type 2 diabetic women. These authors described that moderate to severe LUTS in 36.7% of MetS patients.[19] They also documented that the storage symptoms and total LUTS score were greater in women with MetS when compared to women without Mets. In a study by Gokkaya et al involving 155 postmenopausal women documented that women with MetS had predominant storage symptoms than women without MetS.[3]

Menopause is associated with deleterious changes in body composition and abdominal fat distribution.[20] The increased body fat mass and central adiposity during menopausal transition predispose them to develop MetS.[21] The body mass index and waist circumference are poor predictors of visceral fat which predicts cardio metabolic abnormalities.

Visceral fat is more metabolically active, more sensitive to lipolysis, more resistant to insulin, and has a greater capacity to take up glucose and generate free fatty acids.[22] The gold standard for measuring visceral fat is Computerised Axial Tomography scan (CAT scan) which has its own disadvantages like radiation exposure and costly. DEXA body composition has been validated in comparison to MRI and CAT scan.[23]

The various adipose indices measured are visceral volume, mass and area. Out of this, estimated visceral fat area (cm^2) is the most important as it correlates with the disease risk. Visceral adipose area between 100-160 cm^2 predisposes them to increase risk of heart disease and diabetes. In this study, the estimated visceral adipose area was greater in women with MetS (106.49±39.465) when compared to women without MetS (87.18±32.937)

indicating the women with MetS in this study population were at increased risk of developing heart disease and diabetes.

Body fat percentage is calculated by the ratio of total mass of fat to the total body mass. It consists of both storage body fat and essential body fat. The storage fat consists of fat protecting internal organs in the abdomen and chest. The percentage of essential body fat is generally greater in women (10-13%) when compared to men (2-5%) owing to the demands of child bearing and other hormonal functions. As per obesity definitions, women are considered to be obese with their body fat percentage >25%. In this study, the body fat percentage in women with metabolic syndrome was a mean of 37.3±5 which was higher than women without metabolic syndrome 34.6±3 (p value =0.006).

Lean mass index which is Lean/ht^2, an important index that measures the amount of muscular mass in the body. The higher index reflects more muscle mass while lower index signifies lean skeletal mass. The combination of lean / height and fat mass / height approximates BMI. In this study, the ratio of Lean/Height (Kg/m^2) is greater (P=0.049) in women with MetS (16.3 kg/m^2) compared to women without MetS (15.3 kg/m^2). Similarly, the appendicular lean mass index (Append. Lean/Height^2) is a ratio that measures the lean muscular mass in the extremities (non-trunk) compared to height. There was no difference between two groups in terms of appendicular lean mass indices.

The distribution of body fat (Limb fat/Trunk fat ratio) in elderly persons is a stronger determinant of insulin resistance and adiponectin levels than is trunk fat alone. The visceral fat is a stronger determinant of Insulin resistance.[24] In a study of 166 healthy postmenopausal women, trunk fat was the strongest independent predictor of insulin resistance.[25] However, in this study the trunk/limb fat mass ratio is not very high in both the groups. These women were obese on a whole and have pear shaped obesity rather than an apple shaped metabolically adverse form.

CONCLUSION

64% of post-menopausal women were found to have Mets. LUTS was seen in 52% of postmenopausal women with 90% having filling symptoms. However, there was no statistically significant difference in LUTS in women with and without MetS. There was significant change in body composition among women with MetS as they approach menopause. Just as these women are at increased risk of developing heart disease, diabetes and stroke in their lifetime, they are also at risk of developing LUTS. Creating awareness and encouraging them to change their lifestyle and diet with increased physical activity may minimize the morbidity and mortality due to MetS and improve the quality of life.

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