MENOPAUSE

Body mass index and its correlation to metabolic and hormone parameters in postmenopausal Spanish women

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Abstract

Objective. To assess body weight composition in postmenopausal women and determine correlations with metabolic and hormonal parameters.

Methods. Medical records of 574 postmenopausal Caucasian Spanish women first time attending a menopause clinic were retrospectively reviewed. Retrieved information included general demographic data, type of menopause, time since menopause onset and baseline hormonal and metabolic parameters. A body mass index (BMI) value of ≥ 28.8 kg/m² was used to define obesity. The metabolic syndrome (METS) was diagnosed with three or more criteria: fasting glycemia ≥ 100 mg/dL, high density lipoprotein cholesterol (HDL-C) < 50 mg/dL, triglycerides (TG) ≥ 150 mg/dL, blood pressure ≥ 130/85 mmHg and obesity (as defined above).

Results. Mean age of the whole cohort was 49.9 ± 6.1 years, with 66% having a natural menopause. A 38.9% and 23.1% of all women were obese or had the METS, respectively. Obese women were older, had a higher parity, smoked less, had more time since menopause onset and a higher rate of surgical menopause as compared to non-obese ones (p = 0.001). BMI values positively correlated with age, time since menopause, parity, and glucose, TG and systolic blood pressure levels; displaying an inverse correlation with HDL-C and sex hormone binding globulin (SHBG) levels. SHBG levels inversely correlated with glucose, TG, HDL-C and systolic blood pressure levels.

Conclusion. In this Spanish postmenopausal population BMI significantly increased with age, time since menopause and parity displaying significant correlations with hormonal and metabolic parameters.

Keywords: Body mass index, obesity, postmenopause, hormones, metabolic, sex hormone binding globulin

Introduction

The climacteric is associated to profound bio-psycho-social changes [1,2]. Body fat distribution, weight regulation and adipose tissue hormone secretion are gender related. Abdominal obesity is more frequent among postmenopausal women increasing the risk for: heart disease, hypertension, diabetes, sleep apnea, cancer, osteoarthritis, mental health problems and death [3,4]. Additionally peri- and postmenopausal obesity relates to more severe menopausal symptoms and impaired quality of life [5–7].

Gonadal hormones influence food intake and adiposity [8]. On the other hand, elevated body weight may influence sex hormone binding globulin (SHBG) and sex steroid serum levels [9]. Indeed, in postmenopausal women, SHBG and circulating steroid hormones are influenced by fat/lean mass composition and body weight [10,11], and ethnic differences [12]. Data from animal and human studies indicate that treatment with gonadal hormones may reverse menopausal increased body weight and lean mass loss [13,14]. The objective of the present study was to assess body weight composition in postmenopausal Caucasian Spanish women and determine correlations with metabolic and hormonal parameters.

Material and methods

Study population

The present 10-year retrospective analysis was carried out after approval of the San Cecilio Hospital Ethics Committee. Medical records of postmenopausal women attending for the first time the Menopause Unit of the University of Granada San Cecilio Clinic Hospital (Granada, Spain) were reviewed. All women were consulting due to mild to severe vasomotor symptoms and vaginal discomfort related to atrophy without inflammatory signs. None were on any chronic medication. Menopause was defined as natural (at least one year of spontaneous cease of menses) or induced, by surgery (hysterectomy including bilateral oophorectomy) or either by radiotherapy or chemotherapy. Additionally, estradiol levels < 20 pg/mL were confirmatory.
Recorded information included: age, age at menopause onset, time since menopause (months), parity, marital status, smoking status, type of menopause, baseline laboratory results (hormonal and metabolic), and weight (kg), height (m) and blood pressure recordings (mmHg).

Assessment of body mass index

Body mass index (BMI) was calculated as weight (kg)/squared height (m²). Women with BMI values > 28.8 were defined as obese. This value has been validated in large cohorts, correlating well with abdominal obesity [15,16]. Women were defined as having the metabolic syndrome (METS) if they had 3 or more of the following criteria: fasting glycemia ≥100 mg/dL, high density lipoprotein cholesterol (HDL-C) < 50 mg/dL, triglycerides (TG) ≥150 mg/dL, blood pressure ≥130/85 mmHg and obesity defined by waist circumference [17]. However, instead of using waist circumference for defining obesity (data not available due to the retrospective nature of the study), BMI was used at the cut-off value described above.

Metabolic and hormone serum assays

Basal laboratory work-up included metabolic and hormonal parameters: fasting glycemia, total cholesterol (TC), TG, HDL-C, low density lipoprotein cholesterol (LDL-C), estradiol, and SHBG. TC, TG, LDL-C, HDL-C and glucose levels were assayed with a Hitachi DPP photometric analyzer (Roche Diagnostics GmbH, Mannheim, Germany). Estradiol and SHBG levels were determined using the electrochemiluminescence immunoassay method (Estradiol with Elecsys Estradiol II reagents from Roche Diagnostics GmbH, Mannheim, Germany; and SHBG with Immulite 2000 reagents from Siemens Solutions Diagnostics Limited Gwynedd, UK). Analytic sensitivity and accuracy was 5.0 pg/mL and 2.6% and 0.02 nmol/L 6.6% for estradiol and SHBG, respectively.

Statistical analysis

Statistical analysis was performed using SPSS statistical package (Version 13.0 for Windows, SPSS, Chicago, IL, USA). Data are presented as mean ± standard deviations, percentages, medians, and interquartile ranges. Normal distribution was determined with Kolmogorov Smirnov’s test and according to this, continuous data were compared with Student’s T test (parametric) or the Mann–Whitney test (non parametric). Levene’s test was used to determine variance equality. Chi-square and Fisher’s exact tests were used to compare percentages. Pearson’s or Spearman’s correlation coefficients were used to determine linear relationships among metabolic/hormonal parameters and several continuous variables: age, time since menopause onset, parity and BMI values. A p value of <0.05 was considered as statistically significant.

Results

During the study period a total of 640 postmenopausal women seeking healthcare were attended at the Menopause clinic. Medical records of 66 women were excluded due to incomplete data leaving 574 complete records for statistical analysis. Baseline characteristics of studied women are depicted on Table I. Mean age of the whole study population was 49.9 ± 6.1 years with 66% having a natural menopause. A 38.9% of all women (n = 223) were defined as obese who were significantly older, had higher parity, smoked less, had more time since menopause onset and a higher rate of surgical menopause as compared to non obese ones. Additionally obese women were older at the time of menopause onset (52.5 ± 65.0 vs. 38.0 ± 43.8, p = 0.001).

Hormonal and metabolic parameters found among studied women are depicted in Table II. A 23.1% (n = 133) of all studied women met diagnostic criteria for the METS. Baseline BMI of all women was 27.9 ± 4.6, with 21.4% having hyperglycemia, 16.9% high TG levels, 15.9% low HDL-C and 69% high systolic/diastolic blood pressures. The METS was found more frequently among obese women who also presented higher baseline glucose, TG, LDL-C, and blood pressure levels when compared to non obese ones. Additionally obese women presented significantly lower SHBG and HDL-C levels. Although more obese women had surgical menopause; SHBG levels were similar independent of the type of menopause (Data not shown in Table). Coefficient correlations for metabolic/hormonal parameters and various continuous variables are presented in Table III. BMI values positively correlated with age, time since menopause, parity, and glucose, TG and systolic blood pressure levels; displaying an inverse correlation with HDL-C and SHBG levels.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>All, n = 574</th>
<th>Obese, n = 223</th>
<th>Non-obese, n = 351</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.9 ± 6.1</td>
<td>51.4 ± 5.8</td>
<td>49.0 ± 6.2</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Parity</td>
<td>2.6 ± 1.6</td>
<td>3.0 ± 1.7</td>
<td>2.4 ± 1.5</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Married status (%)</td>
<td>471 (82.1)</td>
<td>190 (85.2)</td>
<td>281 (80.0)</td>
<td>0.11b</td>
</tr>
<tr>
<td>Smoking habit (%)</td>
<td>40 (7)</td>
<td>3 (1.3)</td>
<td>37 (10.6)</td>
<td>0.001b</td>
</tr>
<tr>
<td>Type of menopause (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Natural</td>
<td>379 (66.0)</td>
<td>136 (61.0)</td>
<td>243 (69.2)</td>
<td>0.04b</td>
</tr>
<tr>
<td>Surgical</td>
<td>189 (32.9)</td>
<td>86 (38.6)</td>
<td>103 (29.3)</td>
<td>0.02b</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>4 (0.7)</td>
<td>0 (0)</td>
<td>4 (1.1)</td>
<td>0.16c</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>2 (0.3)</td>
<td>1 (0.5)</td>
<td>1 (0.3)</td>
<td>0.62c</td>
</tr>
<tr>
<td>Age at menopause onset (years)</td>
<td>46.2 ± 5.7</td>
<td>47.0 ± 5.1</td>
<td>45.7 ± 6.0</td>
<td>0.01a</td>
</tr>
<tr>
<td>Time since menopause onset (months)</td>
<td>43.7 ± 53.5</td>
<td>52.5 ± 65.0</td>
<td>38.0 ± 43.8</td>
<td>0.001a</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviations, percentages (%) or [median, interquartile range]. *p value obtained with Mann–Whitney test, chi-square test or Fisher’s exact test when comparing women with and without obesity.
Table II. Hormonal and metabolic parameters among studied women.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>All, n = 574</th>
<th>Obese, n = 351</th>
<th>Non-obese, n = 223</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean baseline BMI kg/m²</td>
<td>27.9 ± 4.6</td>
<td>32.0 ± 3.0</td>
<td>22.9 ± 2.4</td>
</tr>
<tr>
<td>Metabolic syndrome (%)</td>
<td>28.8</td>
<td>35.5</td>
<td>22.4</td>
</tr>
<tr>
<td>SHBG &lt; 34 nmol/L (%)</td>
<td>20.3 ± 2.0</td>
<td>19.5 ± 2.2</td>
<td>22.3 ± 3.6</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>150 (%)</td>
<td>160 (%)</td>
<td>150 (%)</td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>50 (%)</td>
<td>50 (%)</td>
<td>50 (%)</td>
</tr>
<tr>
<td>Blood pressure ≥130/85 mmHg (%)</td>
<td>306 (60.1)</td>
<td>328 (66.0)</td>
<td>302 (52.5)</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviations, percentages (%) or median, interquartile range; *p* value obtained with Mann–Whitney test, Student’s *t* test or chi-square test when comparing women with and without obesity; SHBG, sex hormone binding globulin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Discussion

Body weight increases with age and relates to metabolic and hormonal changes that significantly increase health related risks [4,5]. Although many publications have used traditional BMI cut-off values to define overweight (>25 kg/m²) and obesity (>30 kg/m²), the present study used 28.8 kg/m² to define obesity. Various reports have validated this value as a predictor of cardiovascular risk [15,16], and also pointed out to the fact that BMI is a major determinant of body fat accretion during the menopausal transition [18]. In addition, postmenopausal women display complex interrelationships between BMI, glucose, lipid and SHBG levels and increased cardiovascular risk. The present study was drawn upon Caucasian postmenopausal women from the Southern part of Spain (Granada) where a traditional Mediterranean lifestyle is generally followed [19]. It was found that more than one third was obese which is similar to the prevalence found in the general Spanish population [20,21]. Independent of the type of menopause, our obese women were older, had more time since menopause onset and a higher parity than those non-obese. These figures were confirmed by significant coefficient correlations and are consistent with the findings of others pointing out to the fact that in mid-aged women BMI increases in direct relation to age and time since menopause onset [22–25]. Contrary to our findings, the longitudinal Massachusetts Women’s Health Study found no relationship between weight gain and the menopause [26].

Hormonal fluctuations, observed during women’s life span and female gender specific events (i.e. number of pregnancies and the menopausal transition), may partly explain gradual weight gain and increasing obesity rates seen during the menopausal transition. Despite this, the effect of the menopause could be seen as small in comparison to other influences such as age, physical activity, chronic stress and comorbidities [27–31]. In the general population, parity and obesity are strongly age dependent yet also influenced by many other cofactors such as education, occupation, socio-economic status, working capacity, smoking habit, exercise and lifestyle variables. Reports indicate that obesity prevalence for a determined age segment is related to parity [32,33]. This indeed is in agreement with the significant correlation found in our series between parity and BMI. Despite the aforementioned, reports indicate that psychosocial factors may not totally explain the effect of childbearing over body weight [34,35]. Fat accumulation, insulin resistance and glucocorticoid secretion observed during pregnancy, as well as fewer ovulatory cycles in multiparas, may possibly explain the obesity/parity correlation. Additionally one cannot omit the fact that infant care produces changes in physical activity, diet and social habits. Indeed, women tend to gain weight and fat with succeeding pregnancies, decreasing hip and thigh while increasing waist circumference, resulting in a relative decrease in lower-body fat. When fat is regained after the postpartum period, relatively more is stored in central vs. peripheral depots, resulting in a patterned change in body shape with parity [36]. Co-morbid conditions prevalent after the menopause (i.e. osteoarthritis, degenerative lumbar, spondylolisthesis) [37,38] related to body aches and pain, may favor mobility limitation, reduced physical activity and hence body weight gain [39]. Depression and anxiety are frequent in mid-aged
women, especially among those postmenopausal and obese [40,41]. Psychosocial stressors are also factors that increase weight gain [42].

In the present series, BMI negatively correlated with HDL-C and SHBG levels and positively with glucose, TG and systolic blood pressure levels. Our findings support those of Akin et al. [43]. Obesity is the most prevalent cluster of all composing the METS [44]. METS, on the other hand, would be more prevalent among obese women, as it was the case in the present series. Although the menopause may favor glucose and lipid profile alterations and diabetes or hypertension risk, if it is not accompanied by other cardiovascular risk factors independently of age, its stigma as a risk factor should cease [45]. Contrary to this, obesity relates to different metabolic alterations, diabetes and hypertension [46]. Glucose levels in obese women of the present series were significantly higher fact that positively correlated with age and negatively with SHBG levels. Elevated fasting glycemia is the expression of complex metabolic alterations which contribute to insulin resistance [47]. In obese women, reduced muscle activity may affect body weight and secondarily alter glucose metabolism, insulin resistance and other metabolic changes [48]. Contrary to this, regular exercise may maintain lean mass [49,50].

TG, HDL-C and LDL-C levels are influenced by BMI [44,51]. In accordance to this, obese postmenopausal women of the present series displayed significantly higher serum TG and LDL-C and lower HDL-C levels. TG levels significantly correlated with age and BMI and negatively with SHBG levels; whereas HDL-C levels negatively with BMI and SHBG levels. Our findings demonstrate the negative metabolic effects of obesity. Although lipid profile may worsen with age, BMI is still a major determinant. Indeed, previous studies with serial measurements have reported that BMI and lifestyle are major contributors of lipid alterations including increases in TC, LDL-C and TG levels [52,53]. In our studied postmenopausal population, obese women displayed a significantly higher METS rate than non obese ones (52.5% vs. 4.6%). This emphasizes the importance of obesity in the pathogenesis of the METS. Reports indicate that multiparity increases the risk for the METS [54,55], although the association decreased after BMI adjustment [54] suggesting that weight may be an important mediator of the effect that parity has over the risk of developing the METS.

Mild increases in systolic and diastolic blood pressure may be seen during the menopausal years [56]. Hypertension prevalence in our cohort was high and significantly higher in obese women. Interesting is the fact that this prevalence is higher than that reported in other Spanish studies [57]. This could be related to the high rate of surgically induced menopause, undiagnosed hypertension cases or disparity in diagnostic criteria, individual awareness of the importance of hypertension or other unidentified factors [58]. In our series age and time since the menopause positively correlated to BMI values and mean systolic and diastolic blood pressures. Previous studies have reported that the menopause does not affect blood pressure per se or it has a minimal influence [59]. Hypertension after the menopause appears to be more related to increased BMI and aging, co-morbid conditions (not related to the menopause), lifestyle and low physical activity [31,59]. Moreover, several reports support the fact that increased blood pressure levels, mortality and morbidity rates seen in postmenopausal women are mostly related to age [60,61]. We additionally found a significant correlation between hypertension and parity. In one study a mild negative relationship has been seen between the number of pregnancies and blood pressure [62]. Hypertensive disorders during pregnancy are associated with higher blood pressure later in life [63], and early age at first delivery increases the risk of isolated systolic hypertension [64].

SHBG has high-affinity for testosterone and to a lesser extent for estradiol; thus regulating their serum levels, bioavailability for target cells and mutual balance [65]. In one study, SHBG declined steadily with age with a modestly greater rate of change observed between 49 and 54 years while the free androgen index increased from 1.3 to 2.5 from 34 to 58 years [66]. Reduction in caloric intake and weight loss increases SHBG levels, regardless of food composition [67]. Serum SHBG levels of our postmenopausal series inversely correlated to BMI, glucose, TG, HDL-C and systolic blood pressure levels. These findings are closely similar to those reported by others [68,69]. It may seem that SHBG plays a central role in modulating the clusters of the METS [70,71]. Indeed as it has been reported, lower SHBG levels (obesity or carriers of a SHBG single nucleotide polymorphism) are associated with an increased risk of type 2 diabetes, suggesting a causal role for SHBG [72,73]. Moreover among postmenopausal obese women SHBG levels negatively correlated with fasting glucose, postprandial glycemia and positively with HDL-C, with significant inverse associations with the clusters of the METS [43].

Finally, regarding the limitations of the present study one can mention its retrospective design. Despite this, two strengths can be identified: first it uses updated criteria for defining obesity and the METS and second it confirms recent observations that BMI correlates with metabolic and hormonal parameters. Prospective longitudinal studies are warranted in this sense.

It may be concluded in accordance to the results of this retrospective study that in a rather homogenous Spanish postmenopausal population BMI significantly increased with age, time since menopause and parity displaying significant correlations with hormonal and metabolic parameters. In light of these facts, weight gain prevention should be recognized as an important health goal for women before they approach the menopause. A healthy lifestyle, appropriate diet and physical activity may be an

<table>
<thead>
<tr>
<th>Body mass index</th>
<th>Estradiol</th>
<th>SHBG</th>
<th>Glycemia</th>
<th>TG</th>
<th>HDL-C</th>
<th>Systolic blood pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.23 (0.001)</td>
<td>−0.02 (0.69)</td>
<td>−0.01 (0.94)</td>
<td>0.20 (0.001)</td>
<td>0.17 (0.001)</td>
<td>−0.02 (0.79)</td>
</tr>
<tr>
<td>Time since menopause</td>
<td>0.13 (0.003)</td>
<td>0.02 (0.64)</td>
<td>0.02 (0.65)</td>
<td>0.08 (0.07)</td>
<td>0.08 (0.08)</td>
<td>−0.01 (0.96)</td>
</tr>
<tr>
<td>Parity</td>
<td>−0.07 (0.11)</td>
<td>−0.26 (0.001)</td>
<td>0.20 (0.001)</td>
<td>0.23 (0.001)</td>
<td>−0.19 (0.001)</td>
<td>0.37 (0.002)</td>
</tr>
<tr>
<td>SHBG</td>
<td>0.30 (0.59)</td>
<td>−0.04 (0.03)</td>
<td>−0.06 (0.15)</td>
<td>0.07 (0.13)</td>
<td>0.06 (0.20)</td>
<td>−0.03 (0.55)</td>
</tr>
</tbody>
</table>
important cost effective, although difficult to maintain, way of preventing many chronic conditions that relate to elevated body weight.

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References


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