

Research Article

Metabolic Syndrome Component Changes Over a Decade, During the Menopausal Transition in Tehranian Women: Tehran Lipid and Glucose Study (TLGS)

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Abstract

Background: Metabolic syndrome (MetS) is a group of risk factors that increase the risk of heart diseases, diabetes, and strokes.

Objective: This study was conducted to assess the MetS component changes over a decade, during the menopausal transition in Tehranian women.

Methods: In a cross-sectional study, 1,999 subjects were selected from 15,005 participants of the Tehran Lipid and Glucose Cohort Study (TLGS), who have further assessed for MetS components changes over a decade (2007–2017). We excluded 596 smokers and those who were current users of any hormone replacement therapy or oral contraceptives. 1403 women aged between 15–65 years, among all the participants of the TLGS, were classified into three groups: 1. Pre-M (pre-menopausal) women, aged between 45–49 years, 2. M (menopausal) women, with a permanent cessation of menses of less than 12 months and more than 3 years, and 3. Post-M (post-menopausal) women, who have had a history of a minimum of 3-years of cessation of menses. All the components of MetS were evaluated, following the age adjustment factor, according to the ATPIII criteria.

Results: The mean ages of pre-M, menopausal, and post-M groups were 46.8 ± 1.4 , 52.8 ± 3.1 , and 58.7 ± 4.9 years, respectively. The prevalence of the metabolic syndrome was 33.9%. All the groups demonstrated an increase in the waist, and systolic blood pressure ($p < 0.001$). Odd's ratio, confidence interval, and the significance of some of the metabolic syndrome components were: Fasting plasma glucose (OR: 1.031, CI: 1.009-1.054, $P < 0.005$), 2-hour blood glucose (OR: 1.011, CI: 1.004-1.018, $P < 0.003$), triglyceride (OR: 1.023, CI: 1.019-1.028, $P < 0.002$), HDL-c levels (OR: 0.89, CI: 0.865-0.918, $P < 0.005$), and waist circumference (OR: 1.044, CI: 1.006-1.083, $P < 0.022$).

Conclusion: Over a decade, during the menopausal transition, the waist circumference and systolic blood pressure were associated with an increase in the metabolic syndrome.

Keywords: Metabolic syndrome; Menopause; Aging; TLGS

Introduction

MetS is a group of risk factors that increase the risk of heart diseases, diabetes and, strokes, with a prevalence rate of 13.8% to more than 60.0% in various populations [1-4]. Menopausal transition is considered to be a risk factor for MetS, probably due to the decreasing estrogen levels and increasing insulin resistance, secondary to the menopause determinates [3,5,6]. Additionally, post-menopause, as a period of hyperandrogenism due to ovarian failure, is accompanied by increasing levels of LDL and decreased levels of HDL cholesterol, associated with MetS [7,8]. Independent of age,

postmenopausal and premenopausal periods have higher triglyceride and lower high-density lipoprotein cholesterol (HDL-C) levels [9]. Some studies [10,11], after age adjustment, showed no significant differences among the mentioned components. Longitudinal studies showed the same results [12,13]. One study in Japan showed that menopause was associated with an increase in the total cholesterol levels or in the level of blood pressure [14]. Our previous study, ten years ago, showed that the frequency of MetS was significantly higher in post-M women as compared to pre-M women; low HDL-c and high diastolic blood pressure was the most frequent feature in comparison to the other factors [15]. We aimed to use the data of TLGS to assess the MetS components changes over a decade, during the menopausal transition in Tehranian women.

Methods

In a cross-sectional study, 1999 subjects were selected from 15005 participants of the Tehran Lipid and Glucose Cohort Study (TLGS) [16], who have further assessed for MetS components changes over a decade (2007–2017). We excluded 596 smokers and those who were current users of any hormone replacement therapy or oral contraceptives. 1403 women aged between 15–65 years, among 1999 participants of the TLGS, were classified into three groups: 1. Pre-M (pre-menopausal) women, aged between 45–49 years, 2. M (menopausal) women, with a permanent cessation of menses of less than 12 months and more than 3 years, and 3. Post-M (postmenopausal)

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women, who have had a history of a minimum of 3-years of cessation of menses. All the components of MetS components were evaluated, following the age adjustment factor, according to the ATPIII criteria definition, 1) TG \geq 150 mg/dl, 2) High-density lipoprotein cholesterol (LDL-C) $<$ 50 mg/dl, 3) BP \geq 130/85 mmHg, 4) FBG \geq 100 mg/dl, and WC $>$ 88 cm. The study protocol was approved by the independent ethics committee and was conducted in accordance with the declaration of the Helsinki guideline. All the subjects were provided with a consent letter before the screening. Demographic and social information was obtained on the basis of a questionnaire. Blood pressure was measured twice, through the right arm, after a 15-min rest in the sitting position, using a standard mercury sphygmomanometer, calibrated by the Iranian Institute of Standards and Industrial Researches. Abdominal obesity was defined as a waist circumference $>$ 88 cm. A morning blood sample was collected from the subjects after 12 hr 14 hr of overnight fasting and an additional blood sample was obtained 120 min after the oral administration of an 82.5 g glucose monohydrate solution (equivalent to 75 g anhydrous glucose). Subsequent blood samples were taken in the sitting position, according to the standard protocol, and centrifuged within 30 min 45 min of collection. All the blood glucose analyses were carried out at the TLGS research laboratory on the day of blood collection by the Selectra 2 auto-analyzer (Vital Scientific, Spankeren, Netherlands). Glucose was measured using an enzymatic (glucose oxidase) colorimetric method, by a commercial kit (Pars Azmun Inc. Tehran Iran). Assay performance was monitored, following every 20-tests, using the glucose control serum, precinorm (normal range), and precipath (pathologic range), wherever applicable (Boehringer Mannheim, Germany). The glucose standard calibrator, for the automated system (Roche, Germany), was regularly used to calibrate the Selectra 2 auto-analyzer for each day of laboratory analyses. All the samples were analyzed only when the internal quality control met the acceptance criteria. Inter- and intra-assay coefficients of variation are both 2.2%. The result of the oral glucose tolerance test of each subject was used to classify the glucose metabolism status, according to the WHO criteria. Serum total cholesterol levels and HDL were measured by cholesterol oxidase phenol aminoantipyrine (CHOD-PAP), and the triglycerides by glycerol-3 h postprandial glucose were also assessed after a consumption of 75 g of glucose by the glucose oxidase phenol aminoantipyrine (GOD-PAP) enzymatic method, within a normal range of 75 to 100 mg/dl. Statistical analyses were performed using the Statistical Package for Social Sciences (Version 16.0; SPSS, Chicago). The analysis was done using Logistic regression, Pearson's chi-square statistic Student's t-test, ANOVA, followed by a post hoc method. P-value $<$ 0.05 was considered significant.

Results

The mean ages of pre-M, menopausal and post-M groups were 46.8 ± 1.4 , 52.8 ± 3.1 , and 58.7 ± 4.9 years, respectively. The prevalence of metabolic syndrome was 33.9%. Table 1 shows that SBP, among the Post-Menopausal group, was significantly higher than Pre-Menopausal ($p < 0.01$) and Menopausal groups ($p < 0.04$). The waist circumference, among the Post-Menopausal group, was significantly higher than the Pre-Menopausal group ($p < 0.01$).

A logistic regression was performed to ascertain the effects of menopausal status (three groups of participants) on the likelihood of developing the metabolic syndrome. The non-metabolic syndrome was considered to be the reference group. During a decade, a potential risk of MetS had occurred via systolic blood pressure, FBS, BS2hr,

TG, Weight, and WC rising. HDL had a protective role against Mets, among the metabolic syndrome subjects (Table 2).

Discussion

Findings showed that the prevalence of metabolic syndrome was 33.9%. Systolic blood pressure (SBP), among the Post-Menopausal group, was significantly higher than the Pre-Menopausal and Menopausal groups. The waist circumference of the Post-Menopausal group was significantly higher than the Pre-Menopausal group. During a decade, a potential risk of MetS had occurred via systolic blood pressure, FBS, BS 2 hr, TG, Weight, and WC rising. HDL had a protective role against Mets, among the metabolic syndrome subjects.

According to studies from different countries, the prevalence of MetS in women has ranged from 15.9% in Thai women [17] to 26.4% in Iranian women [18], and 33.8% in Puerto Rican women [19]. In line with our findings, Gurka, et al. [20] showed that the rate of the severity of MetS, during the menopausal transition, was on a rapid increase and a decrease, afterward. They concluded that the triglyceride levels could play a major role. Marjani, et al. [21] showed that in comparison to other metabolic components, increases in WC and BP were the most frequent characteristics. Based on the American Association of Clinical Endocrinologists guidelines, women with MetS, WC, and BMI are more accurate predictors of HDL-C concentrations [22]. The findings of the study were in line with the Marjani study. In contrast to the findings of the study, Guthrie

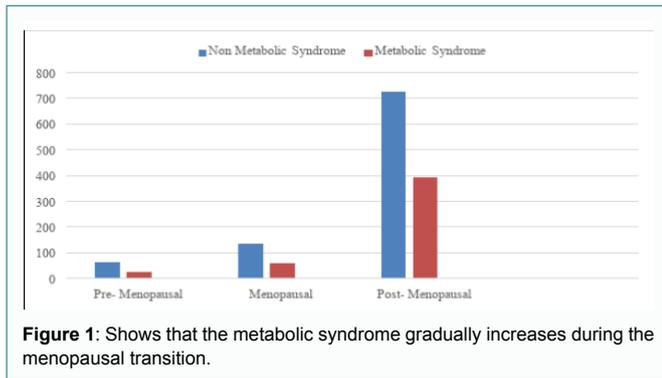
Table 1: Comparison of metabolic syndrome risk factors among Pre-Menopausal, Menopausal, and Post-Menopausal groups.

Variables	Pre-Menopausal N=88	Menopausal N=197	Post-Menopausal N=1116
SBP(mmHg)	116.07 \pm 15.05*	122.06 \pm 17.84	125.55 \pm 19.72**
DBP(mmHg)	78.17 \pm 9.25	80.99 \pm 10.90	79.82 \pm 10.37
FBS(mg/dl)	107.59 \pm 34.03	107.76 \pm 36.17	111.70 \pm 38.03
BS2hr(mg/dl)	118.51 \pm 48.87	123.29 \pm 41.04	127.91 \pm 44.31
TG (mg/dl)	158.82 \pm 89.08	166.96 \pm 100.52	160.45 \pm 80.34
HDL(mg/dl)	54.15 \pm 13.97	52.53 \pm 11.77	52.68 \pm 12.67
WC (cm)	95.32 \pm 10.17	98.30 \pm 12.38	99.24 \pm 11.82**

*P<0.04 Pre-Menopausal compare with Menopausal
**p<0.01, Pre-Menopausal compare with Post- Menopausal

Table 2: Age-adjusted comparison of metabolic syndrome components changes in Non- Metabolic Syndrome and Metabolic Syndrome groups.

Variables	EXP (B)	95% C.I. for EXP(B)	P value
Age (year)	1.059	1.010-1.110	0.018
Reference: Non- Metabolic Syndrome	-	-	-
FBS (mg/dl)	1.031	1.009-1.054	0.005
BS2hr(mg/dl)	1.011	1.004-1.018	0.003
Cholesterol(mg/dl)	1	0.994-1.006	0.977
TG (mg/dl)	1.023	1.019-1.028	0.001
HDL(mg/dl)	0.891	0.865-0.918	0.001
Weight (kg)	1.073	1.051-1.096	0.001
WC (cm)	1.044	1.006-1.083	0.022
Systolic blood pressure	1.031	1.022-1.038	0.001
Diastolic blood pressure	1	0.994-1.023	0.263



reported that there was no difference in normal fasting glucose between the Pre-M as compared to the menopausal women. They found that weight gain had a stronger influence on the development of impaired fasting glucose than menopause itself [23]. Fernandez, et al. [2] showed that WC and BMI were better predictors of HDL-C concentrations among women with MetS. The waist circumference increased over a decade and our findings have been consistent with the prior study findings [24]. In contrast to our findings, Gurka, et al. [20] showed that the waist circumference did not significantly change during the menopausal period. In agreement with the findings of our study, Afzal, et al. [25] reported that HDL-C had decreased in Post-M women compared to pre-M women. Sharma, et al. [3] findings were partly in contrast to the study findings. They showed that a protective mechanism and the effects of biomarkers could be associated with menopause.

Male hormones play an important role, both in young and in menopausal women. Postmenopausal women suffer from a number of menopausal symptoms. After menopause, the total testosterone production decreases, due to a decreased primary and endrusionidion environmental conversion. Metabolic syndrome is directly associated with increasing testosterone activity [26,27].

Janssen, et al. [28] showed that independent of aging, the incidence of the MetS increased from 6 years prior to 6 years post menopause. This association was reported by epidemiologic studies as well. Evidence showed multiple risk factors for the emergence of CVD in the postmenopausal period; however, metabolic syndrome may be present even before menopause [29,30]. Metabolic changes with menopause led to a better recognition of the appropriate interventions for the treatment of women at a risk of future CVD [31]. To identify the relationship between the syndrome metabolic components and coronary heart diseases, further studies must be conducted among different ethnic groups (mostly in low and middle-income countries) [32,33]. Cho, et al. [34] showed that for the metabolic syndrome, postmenopausal status is an independent risk factor. Eshtiaghi, et al. [35] showed that menopause was an independent predictor to the metabolic syndrome.

It seems that the alarming prevalence of MetS worldwide varies, based on populations, lifestyle statuses, and socioeconomic factors. Healthcare must provide a useful tool to identify postmenopausal women who are at a high risk of developing MetS. This study had major strengths in following a large cohort, longitudinally, and assessing the novel markers of the severity of MetS, which were ignored by most studies. The frequency of MetS is significantly higher in the menopausal and post-menopausal period. Some factors, which may influence the severity of MetS, could not be considered. This could, however, be considered as a study limitation.

Conclusion

It can be concluded that the frequency of MetS is significantly higher in post-menopausal women as compared to the other groups. The waist circumference and systolic blood pressure was the most frequent feature in comparison to the other factors. We should target the waist circumference and the systolic blood pressure, by bringing out the changes in lifestyle and dietary habits, to decrease the higher prevalence of MetS and the risk of cardiovascular diseases. Women with MetS are at an increased risk of heart diseases and possibly diabetes than their older counterparts. Based on the results of this study, it is suggested that in the provision of healthcare services and the formulation of clinical guidelines, in addition to the age category, the topic of menopause could be considered as an independent factor affecting the metabolic syndrome.

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