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Assessment of metabolic syndrome and associated cardiovascular risk in post-menopausal women: A longitudinal cohort study

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Abstract
Background: Metabolic syndrome (MetS) is a cluster of metabolic abnormalities, including central obesity, insulin resistance, dyslipidemia and hypertension, which significantly elevate the risk of cardiovascular diseases and type 2 diabetes mellitus. Postmenopausal women are particularly susceptible due to hormonal changes, especially estrogen deficiency, which adversely impacts metabolic health. This study aimed to assess the prevalence of MetS and its associated cardiovascular risk among postmenopausal women in Punjab, India.
Methodology: A longitudinal cohort study was conducted on 275 postmenopausal women aged 45 to 65 years. Data were collected through a standardized proforma including demographic, anthropometric, biochemical and physiological parameters. Blood samples were analyzed for fasting glucose, triglycerides and high-density lipoproteins (HDL). MetS was diagnosed based on International Diabetes Federation (IDF) criteria. Statistical analysis was performed using independent sample t-tests with a significance level of $p<0.05$.
Results: Women with metabolic syndrome showed significantly higher anthropometric measures and adiposity parameters compared to non-MetS subjects ($p<0.05$–$p<0.001$; $t=3.27$–7.53). Obesity indices, including BMI and WHR, were also significantly elevated ($p<0.01$–$p<0.001$). Fasting plasma glucose was significantly higher at follow-ups ($p<0.05$–$p<0.001$), while triglycerides were elevated but non-significant. HDL levels declined non-significantly and blood pressure differences remained statistically non-significant ($p>0.05$).
Conclusion: The study demonstrated a strong association between metabolic syndrome and increased cardiovascular risk in postmenopausal women. It can be concluded that early detection, lifestyle modification, and timely clinical interventions are essential to reduce disease burden and improve long-term health outcomes in this vulnerable population.

Keywords: Adiposity, anthropometric**,** cardiovascular risk, insulin resistance, lipid profile

Introduction

Metabolic syndrome (MetS) is a group of metabolic abnormalities including central obesity, dyslipidemia, hypertension and insulin resistance (IR). It was first named syndrome X due to its interconnectedness with the cardiovascular disease (CVD) [1]. Metabolic syndrome has been significantly linked to increased risk of developing serious non-communicable diseases, such as cardiovascular disease (CVD), stroke and type 2 diabetes mellitus (T2DM) [2]. The occurrence of these diseases depend on several factors, including central obesity (excessive fat around abdomen assessed by waist circumferences) [3], insulin resistance (consequent elevated blood glucose levels) [4], dyslipidemia (high triglyceride levels along with low high density lipoproteins and elevated low density lipoprotein levels) [5]. Other secondary factors responsible for MetS, especially for cardiovascular disease are elevated serum C-reactive protein (CRP) and fibrinogen levels [6]. The overall prevalence of MetS is around 25% throughout the globe, with variations in genetic, environmental and lifestyle factors [7, 8]. The developed countries have had a higher prevalence of metabolic syndrome, while there is an increasing trend in developing countries [6, 9]. The individuals with metabolic syndrome have three times more chances to get a heart attack compared to the people without metabolic syndrome [10, 11].

Menopause is the most important biological and physiological event in a women's life [12]. It has been described that menopausal status is strongly related to an increased risk of the syndrome even after adjusting for confounding variables such as age, body mass index, level of income and physical activity [11, 13]. It is all due to the deficiency of hormone "estrogen" [13, 14]. This deficiency plays a crucial role in the development of MetS, which further increases the risk of CVDs and hypertension [15]. Besides these hormones, aging also plays an important role in the deterioration of metabolic profile [16, 17]. In post-menopausal women, older age, physical inactivity, menopausal age, obesity and hypertension increase the risk of the metabolic syndrome[18, 19] which further increase their vulnerability for CVDs [20, 21]. Menopausal status is also independently associated with central adiposity and lipid profile [22]. Although both the sexes may have abnormal levels of lipid profile and greater waist circumferences, but some studies have concluded that there is a higher prevalence of MetS in males than age-matched pre-menopausal women [23, 24]. However, after menopause this equations does not exist and the prevalence gains its peak towards the women who are above sixty years of age [25]. This study has highlighted the risk of cardiovascular disease in post-menopausal women with metabolic syndrome and without metabolic syndrome.

There are many diagnostic criteria to rule out the metabolic syndrome. In the present study, all the parameters were considered according to International Diabetes Federation (IDF) criteria [26]. MetS was diagnosed through this criteria when the patients presented central obesity (standard race and gender specific waist circumference cut-offs) plus any

two of the four parameters, that were: raised triglycerides (≥150 mg/dl), reduced HDL cholesterol (<40mg/dl in males and <50mg/dl in females), raised blood pressure (systolic ≥130 mm Hg or diastolic ≥85 mm Hg) or raised fasting plasma glucose (≥100mg/dl or previously diagnosed with type 2 diabetes mellitus) [27].

Material and Methods

A longitudinal cohort study was conducted in the Barnala district of Punjab, India on a sample of 346 post-menopausal women, out of which 25 females were excluded from the study due to unavailability of blood samples, from remaining 321 subjects, 46 females were excluded at different levels of the study, due to voluntary withdrawal (30), migration (9), mortality (2) and breast cancer (5). So, the final analysis was done on 275 subjects in the age group of 45 to 65 years to assess the risk of cardiovascular diseases among women with any metabolic syndrome, by comparing with subjects without any metabolic syndrome. The data was collected from door to door survey through a standardized proforma comprising all the vital details including demographics, anthropometric measurements, family history of diabetes and heart diseases, types of medicines and duration of the disease. The post-menopausal women who had been residing in the urban areas of Barnala district of Punjab for at least 10 years and had attained menopause at least 5 years back were included in the study, while the subjects not suffering from any disease other than type 2 diabetes mellitus (T2DM) and high blood pressure; neither undergone hormone replacement therapy (HRT) nor taking insulin were excluded from the study. An intravenous blood sample of 3ml was taken from each subject in a clot activator vial by a trained laboratory technician and transported in an ice box to laboratory. Before collecting the blood samples, an informed consent was taken from each subject and ethical permission was taken from Institutional Clinical Ethical Committee of Punjabi University Patiala. After sample collection, serum was separated from the blood for measuring concentrations of high density lipoproteins, triglycerides and fasting blood sugar by using Erba kits and semi-automated biochemical analyzer.

The parameters included in the study were gross body measurements (height and weight), circumferences (upper arm, waist, hip and thigh), skinfolds (biceps, triceps and thigh), biochemical parameters (high density lipoprotein, triglycerides and fasting blood sugar), physiological parameters (systolic blood pressure and diastolic blood pressure), adiposity (brachial adipo-muscular ratio, femoral adipo-muscular ratio, mean adipo-muscular ratio percentage of adipose mass and absolute adipose mass) and body indices (body mass index, conicity index and waist hip ratio). Various biochemical and physiological parameters of the study were considered in accordance with IDF criteria [26] for assessing the metabolic syndrome. The standard values for various parameters according to the given criteria were: triglycerides (≥150 mg/dl), low HDL (<50 mg/dl), blood pressure (≥130/85 mmHg) and fasting plasma glucose (≥100 mg/dl).

The collected data were expressed as mean ± standard deviation (SD). Normality of the data was assessed prior to analysis. Inter-group comparisons were performed using independent sample t-test at different stages of the study. A p-value of <0.05 was considered statistically significant. All analyses were carried out using SPSS software and 95% confidence intervals were considered where applicable.

Results

The results were compiled for a total of 275 subjects. Every parameter of the study was recorded at three different levels (initial, first and second follow-up). The subjects were divided into two groups (with and without metabolic syndrome).

According to IDF criteria, the mean values of all the anthropometric measurements including weight, circumferences (upper arm, waist, hip and thigh) and skinfolds (biceps, triceps and thigh) were significantly greater in MetS subjects than the individuals without MetS at three different stages of evaluation (Table 1). The mean values of all the anthropometric measurements increased from the baseline data to the end of the study for MetS individuals. Similar findings have been observed for women without MetS in case of upper arm circumference, triceps and thigh skinfolds. But, the mean values of weight and circumferences (waist, hip and thigh) elevated from the baseline assessment to first follow-up and then reduced at the last level of assessment for the subjects without MetS. However, the mean values of bicep skinfolds decreased from the baseline data to first follow-up, followed by an increase at the end of the study for women without MetS. Statistically non- significant differences have been observed in the mean values of height between the subjects with and without metabolic syndrome at each level of the study.

The concentrations of fasting plasma glucose were significantly greater in MetS women at the first and second follow-ups of the study as compared to their counterparts (without syndrome) (Table 2). The concentrations of triglycerides were greater in MetS individuals than among without MetS, while the concentration of high density lipoproteins reduced from the baseline data to the end of the study for MetS women (50.71 to 43.94 mg/dl). But, women without MetS have shown an increasing trend of high density lipoproteins from the beginning to first follow-up and then reduced at the second follow-up. The levels of fasting plasma glucose and triglycerides declined from the initial stage to first follow-up and then elevated at the next stage of the study for MetS individuals. Similar results have been observed for fasting plasma glucose and triglycerides in the group comprising of females without MetS.

The differences in the mean values of systolic and diastolic blood pressures between the two groups (with and without metabolic syndrome) at three different follow-ups of the study were statistically non-significant (Table 2). The baseline data of post- menopausal women based on IDF guidelines [26] showed that the mean values of both the components of blood pressure were statistical and non-significantly greater in the individuals who were without MetS than their counterparts, however the mean values of both the variables of blood pressure were non-significantly lower in the women who were without metabolic syndrome at the first and second levels of evaluation than their peers (with metabolic syndrome). The mean values of all the parameters of blood pressure decreased from the initial stage to the end of the study for subjects without MetS (SBP 144.23 to 137.14 mmHg and DBP 91.35 to 88.57 mmHg), while the mean values of both the components of blood pressure increased from the baseline data to first follow-up and the decreased to the end of the study for MetS females.

The differences of all obesity indices were statistically significant between the two groups (with and without MetS)

at the beginning of evaluation followed by two follow-ups (Table 3). The mean values of conicity index and waist hip ratio remained almost same for both the groups at three different levels of assessment, however the mean value of body mass index increased from the baseline data to the last follow-up of the study for MetS females.

Table 1: Anthropometric measurements among the postmenopausal women of Punjab at three different levels according to IDF criteria (Alberti *et al*., 2006)

Variables	Initial stage (275)			First follow-up (275)			Second follow-up (275)		
	With MetS (n=249) Mean±SD	Without MetS (n=26) Mean±SD	t- value	With MetS (n=249) Mean±SD	Without MetS (n=26) Mean±SD	t- value	With MetS (n=249) Mean±SD	Without MetS (n=26) Mean±SD	t- value
Height (cm)	154.04±5.34	155.73±5.36	1.53	154.07±5.35	155.58±5.23	1.35	154.11±5.36	155.37±5.17	1.07
Weight (kg)	74.02±12.46	61.81±10.44	5.57***	75.51±13.28	65.04±11.70	4.14***	76.58±13.62	63.57±9.09	6.02***
Circumferences (cm)									
Upper arm	30.76±3.81	27.44±2.89	5.39***	31.62±4.00	28.79±3.27	3.97***	32.24±4.32	29.00±3.03	4.53***
Waist	91.66±8.86	78.98±10.31	6.04***	92.92±8.89	80.96±10.38	5.46***	93.51±9.24	79.38±8.18	7.53***
Hip	109.65±10.52	98.15±7.69	6.97***	111.45±11.02	101.46±10.02	4.62***	113.09±11.34	100.24±7.53	7.18***
Thigh	55.44±5.95	51.21±5.13	3.94***	56.33±6.43	53.88±5.58	2.03*	57.05±6.48	52.86±5.57	3.27**
Skinfolds (mm)									
Biceps	17.90±4.79	14.69±4.44	3.48**	18.71±5.01	13.92±4.21	5.24***	20.62±5.32	17.24±3.95	3.66***
Triceps	26.67±4.87	21.50±3.65	6.64***	29.20±5.67	24.33±4.40	5.03***	32.08±6.38	26.86±6.90	3.35**
Thigh	34.28±7.43	29.46±7.06	3.29**	39.15±8.31	36±7.50	1.95	43.37±8.86	38.76±8.46	2.39*

Significant level *p<0.05, **p<0.01, ***p<0.001 (IDF: International Diabetes Federation, MetS: Metabolic syndrome, n= number of individuals)

Table 2: Biochemical and physiological parameters among the postmenopausal women of Punjab at three different levels according to IDF criteria (Alberti *et al*., 2006)

Variables	Initial stage (275)			First follow-up (275)			Second follow-up (275)		
	With MetS (n=249) Mean±SD	Without MetS (n=26) Mean±SD	t- value	With MetS (n=249) Mean±SD	Without MetS (n=26) Mean±SD	t- value	With MetS (n=249) Mean±SD	Without MetS (n=26) Mean±SD	t- value
FPG	122.63±55.13	113.54±48.62	0.9	119.37±38.60	99.12±22.80	3.85***	126.56±38.27	110.95±31.52	2.14*
TG	165.28±50.17	162.73±40.88	0.3	158.45±47.16	144.79±49.44	1.30	175.20±41.81	168.81±39.20	0.71
HDL	50.71±8.48	49.69±7.55	0.65	48.24±8.23	49.75±8.33	0.85	43.94±6.70	46.00±6.54	1.38
Blood Pressure (mmHg)									
SBP	142.01±14.14	144.23±11.02	0.95	143.23±14.14	138.96±10.21	1.90	140.87±13.40	137.14±15.86	1.05
DBP	90.04±6.78	91.35±7.15	0.89	90.94±6.41	88.54±8.53	1.34	90.31±7.49	88.57±9.64	0.81

Significant level *p<0.05, **p<0.01, ***p<0.001 (FPG: Fasting Plasma Glucose, TG: Triglycerides, HDL: High Density Lipoproteins, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, IDF: International Diabetes Federation, MetS: Metabolic syndrome, n= number of individuals)

The mean values of all the adiposity variables increased from the initial stage to the end of second follow-up in all the subjects. The mean values of brachial adipo-muscular ratio (BAMR), mean of brachial and femoral adipo-muscular ratio (MAMR), percentage of adipose mass and absolute adipose mass were significantly more in MetS women than the individuals without syndrome at the initial and first follow-up stage of the study (Table 3). However, the mean values of femoral adipo-muscular ratio (FAMR) at the initial stage of the study were significantly larger in MetS subjects than without MetS. Statistically non-significant differences have been observed between the two groups (with and without MetS) at the first and second follow-ups of the study for FAMR. Similar results were reported at the second follow-up for all the adiposity indices (except absolute adipose mass).

Table 3: Obesity indices and adiposity parameters among the postmenopausal women of Punjab at three different levels according to IDF criteria (Alberti *et al*., 2006)

Variables	Initial stage (275)			First follow-up (275)			Second follow-up (275)		
	With MetS (n=249) Mean±SD	Without MetS (n=26) Mean±SD	t- value	With MetS (n=249) Mean±SD	Without MetS (n=26) Mean±SD	t- value	With MetS (n=249) Mean±SD	Without MetS (n=26) Mean±SD	t- value
Obesity indices									
CI	1.22±0.07	1.15±0.09	3.68***	1.22±0.07	1.15±0.06	5.37***	1.22±0.07	1.14±0.06	6.15***
WHR	0.84±0.06	0.80±0.06	2.95**	0.84±0.05	0.80±0.04	4.32***	0.83±0.05	0.79±0.05	3.25**
BMI (kg/m^2)	31.21±0.07	25.46±3.75	7.15***	31.82±5.48	26.89±4.61	4.92***	32.26±5.61	26.42±4.19	5.96***
Adiposity									
BAMR	0.69±0.16	0.59±0.12	3.73***	0.73±0.18	0.60±0.08	6.66***	0.83±0.21	0.75±0.25	1.46
FAMR	0.55±0.14	0.50±0.13	1.99**	0.65±0.16	0.60±0.12	1.66	0.74±0.20	0.70±0.18	1.13
MAMR	0.62±0.13	0.55±0.10	3.39**	0.69±0.14	0.60±0.09	4.56***	0.78±0.18	0.72±0.19	1.48
%AM	45.45±9.76	40.08±7.44	3.39**	50.74±10.63	44.13±6.29	4.56***	57.70±13.53	53.07±13.87	1.48
AAM (kg)	33.83±9.79	25.09±8.02	5.17***	38.63±11.33	29.04±8.63	5.04***	44.45±13.26	33.92±10.33	4.38***

Significant level *p<0.05, **p<0.01, ***p<0.001 (CI: Conicity Index, WHR: Waist Hip Ratio, BMI: Body Mass Index, BAMR: Brachial adipo-muscular ratio, FAMR: Femoral adipo-muscular ratio, MAMR: Mean of Brachial and femoral adipo-muscular ratios, % AM: Percentage of adipose mass, AAM: Absolute Adipose Mass, IDF: International Diabetes Federation, MetS: Metabolic syndrome, n= number of individuals)

Discussion

According to IDF criteria, the mean values of waist hip ratio, body mass index and waist circumference were significantly higher among post-menopausal women with MetS as compared to the post-menopausal women without metabolic syndrome at three different stages of the study (Table 1). These results of the study were in agreement with the findings of other studies carried out in Korea, Iran and Punjab [28, 29, 30]. The study has also shown an increasing trend in the adiposity parameters from the baseline to the second follow-up (Table 3), similar results were seen in the studies carried out in California, Karachi, Iran and Saudi Arabia under the broader term "Obesity" [31, 32, 33, 34]. However, the mean conicity index and waist-hip ratio in this study remained almost same throughout the study, whereas the body mass index showed increasing trend from initial to the second follow-up. Due to the increasing trend in most of the adiposity parameters, it can be interpreted that the risk of getting cardiovascular diseases is higher; this is in cognizance with the results of Rexrode *et al.* [35]. Few studies from South Asian populations were consistent with the present study, where central obesity has been identified as a primary driver of metabolic syndrome due to an increased visceral fat accumulation following menopause [9, 36]. Also, there is a two-fold risk for cardiovascular diseases (CVDs) in post-menopausal women [37, 38, 39] and these metabolic abnormalities threaten the human health [18]. Significant greater concentration levels of fasting plasma glucose and triglycerides were reported among post-menopausal women with metabolic syndrome than their counterparts at the first and second follow-up stages (Table 2), similar results have been delineated in other studies between post-menopausal women with and without metabolic syndrome [28, 29, 32, 34, 37]. The significantly elevated fasting plasma glucose levels among women with metabolic syndrome has been seen in this study, showing agreement with previous studies indicating that insulin resistance is a central pathological component of metabolic syndrome, particularly after menopause [40, 41]. Few studies have shown no menopausal effect on triglyceride levels [42, 43], while other studies have manifested elevation of triglyceride levels after menopause [44, 45]. Also, some longitudinal studies have reported inconsistent changes in triglycerides across menopause transition, suggesting that lipid alterations may be influenced by dietary habits and genetic predisposition [46, 47].

The present study has observed non-significant reduction in the HDL levels among the post-menopausal women with metabolic syndrome at the first and second follow-up stage which is in conformity with the earlier studies [28, 29, 32, 34, 37]. An inverse relationship was found between low concentration of high lipoproteins and an increased risk of cardiovascular diseases [48]. The reduction in the concentration level of HDL has been taken into account as one of cardiovascular disease risk factor among post-menopausal women [28, 29, 32, 34, 37]. The mean values of both systolic and diastolic blood pressure in MetS post-menopausal women increased from initiation of the study to the first follow-up, followed by decrease till the end of analysis, as per the IDF criteria. Many studies have shown menopausal effect on both the components of blood pressure in MetS diagnosed women [28, 29, 30, 31, 34], while the study by Bengtsson and Lindquist showed a little reduction in blood pressure after menopause [49].

Conclusion

The present study indicated that postmenopausal women with metabolic syndrome exhibited significantly greater values of anthropometric measurements, obesity indices and adiposity parameters compared to those without the syndrome. The biochemical markers, including fasting plasma glucose and triglycerides were elevated, while HDL levels showed a declining trend over time, reflecting worsening metabolic health. Although blood pressure differences between the groups were statistically non-significant, a general pattern of metabolic imbalance was evident in affected individuals. The progressive increase in obesity and adiposity measures across follow-ups further suggested a growing risk of associated complications. Overall, these findings emphasized a strong link between metabolic syndrome and increased cardiovascular and metabolic risk in postmenopausal women, highlighting the importance of early diagnosis, lifestyle modification and timely clinical intervention to improve long-term health outcomes.

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