Original Article

Metabolic Syndrome and Its Components: A Cross-Sectional Analysis of Its Distribution among Pre- and Post-Menopausal Women from Northern India

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ABSTRACT

Aim: This study aims to determine the prevalence of Metabolic Syndrome (MS) and recognize its abnormal components in pre and postmenopausal women. We also aim to recognize the abnormal components in postmenopausal women with regard to duration since menopause. **Materials and Methods:** The cross-sectional study was undertaken among pre- and post-menopausal women between 40 and 65 years. Women with MS were identified as per the modified National Cholesterol Education Program Adult Treatment Panel III. **Results:** A total of 220 women were enrolled comprising 112 premenopausal and 108 postmenopausal women, the prevalence of MS among them being 33% and 51.85%, respectively. Postmenopausal status was found to be independently associated with MS when adjusted for potential confounders (adjusted odds ratios = 14.77, 95% confidence intervals: 1.77–23.33). All the components were proportionately higher in postmenopausal group, the rise in blood pressure (BP) (P = 0.003) and low high-density lipoprotein (HDL) (0.027) being statistically significant. The risk of MS, abdominal obesity, and high BP were highest in <5 years since menopause and decreased thereafter. The risk for low HDL and high triglyceride increased with the number of years since menopause, reaching the peak level in the 5–9-year group and then decreased while the risk of high fasting blood sugar increased reaching peak in the 10–14 years' group. **Conclusion:** The prevalence of MS is significantly high in postmenopausal women. Screening of women in premenopausal period will give an opportunity to intervene and prevent the menace of MS in Indian women predisposed to abdominal obesity, insulin resistance, and cardiovascular adverse events.

KEYWORDS: *Metabolic syndrome, postmenopausal women, premenopausal women, prevalence, time since menopause*

INTRODUCTION

The metabolic syndrome (MS) or syndrome X, or insulin resistance syndrome is an assemblage of abnormalities of metabolic parameters that can presumably predict the eventual development of type 2 diabetes mellitus (DM) and cardiovascular disease (CVD) in future.[1] The components of MS in women include central obesity (waist circumference [WC] >88 cm), insulin resistance (Fasting Glucose (FG) ≥100 mg/dL), hypertriglyceridemia (Fasting triglyceride [TG] ≥150 mg/dL, hypertension (≥130/85 mmHg), and decreased high-density lipoprotein (HDL <50 mg/dL) cholesterol. As per the modified National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III), the diagnosis of MS is made when three

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or more of the above-mentioned factors coexist.[2] The prevalence of MS increases with age, especially during the period of the menopausal transition. The transition from pre- to post-menopause is associated with the development of many manifestations of MS, such as increased intra-abdominal fat, development of atherogenic lipid profile including increased low-density lipoprotein (LDL) and TGs levels and increased glucose and insulin levels. These changes may be attributed to the direct result of ovarian failure or an indirect result of metabolic consequences of central fat redistribution with estrogen deficiency.[3]

India has around 43 million menopausal women and it is projected that by the year 2026, the menopausal population would increase to nearly 103 million.[4] Indian studies have projected the prevalence of MS from 27.4% to 59.4% in premenopausal and from 16.8% to 65.7% in postmenopausal women.[5,6] The national burden of MS and the possible risk of future development of CVD and Type 2 DM in this subset of women will take a toll on health-care infrastructure. Keeping this in mind, the present study is contemplated to determine the prevalence of MS and recognize its components among pre and postmenopausal women attending a tertiary care hospital in northern India. The secondary aim is to recognize the abnormal components in postmenopausal women with MS with regard to duration since menopause.

Materials and Methods

The cross-sectional study was conducted in the department of obstetrics and gynecology in a tertiary health institute in Northern India for 18 months after approval was taken from the institutional ethical committee. Pre and postmenopausal women in the age group of 40–65 years attending the outpatient department with any gynecological complaints were enrolled for the study after informed written consent was obtained. Women on hormone replacement therapy, those diagnosed with the polycystic ovarian syndrome, secondary hypertension, and having a history of smoking or alcohol intake were excluded from the study.

A detailed history with regard to age, presenting complaint, parity, and menopausal status along with sociodemographic details was elicited. Physical examination was done to measure blood pressure (BP), body mass index (BMI), and WC. Systolic BP and diastolic BP were measured in a sitting position after resting for 10 min, twice at 5 min intervals, using a digital sphygmomanometer, and the average value in mm/Hg was calculated. Height was measured in cm with a tape meter to the nearest 0.1 cm, in a standing position without wearing shoes. Weight was measured to the nearest 0.1 kg using a digital weighing machine with participants in light clothing and without shoes. BMI was then calculated by dividing weight in kilograms by the height in meters squared (kg/m^2). The results of morbidity and mortality derived from the white Caucasian populations will not be an accurate depiction in Asian Indians with a distinct difference in body composition and higher predisposition of developing MS at lower cut off value of BMI. Hence, BMI is classified as per the WHO BMI range for Asian Indians.[7] into: normal – 18.0–22.9 kg/m^2, overweight – 23.0–24.9 kg/m^2, and obese – ≥25 kg/m^2.

WC was measured at midpoint between lower costal margin and iliac crest at end of normal expiration in a horizontal plane using a measuring tape (in centimeters). A venous sample was collected from all the subjects who came after 8–12 h of overnight fasting. Fasting blood glucose (FPG) (mg%) was estimated by the glucose oxidase enzymatic method. Total cholesterol, serum TGs, serum HDL, and serum LDL (mg%) were measured by direct enzymatic method.

The recommended cut off value of WC of >88 cm in women[2] may not be appropriate to apply to populations with diverse ethnicity owing to variation in the mean values of measurements and its characteristically specific association with type 2 diabetes and cardiovascular adverse events.[8] Misra *et al*.[8] observed even with WC cut offs of ≥90cm in men and ≥80cm in Asian women, the odds of developing cardiovascular adverse event is high (4.2 and 2.2, respectively) in those with BMI ≥25 kg/m^2. The higher risk of morbidity with lower WC in Asian Indians is validated by many other studies as well.[9,10] In view of the above considerations, the definitions of MS according to the modified NCEP ATP III criteria.[11] requires any three or more of the following:

1. FPG ≥100 mg/dl (or receiving drug therapy for hyperglycemia)
2. Systolic BP ≥130 mmHg and diastolic BP ≥85 mmHg (or taking drugs for hypertension)
3. WC >80 cm
4. Fasting serum TG ≥150 mg/dl (or receiving treatment for elevated TG)
5. HDL-cholesterol <50 mg/dl (or taking drug therapy for low HDL-C).

Sample size

The overall prevalence of MS among pre- and post-menopausal women by Pandey *et al*.[5] was found to be 56.6%. Assuming this prevalence of 56.6% with 95% confidence interval (CI), 80% power, 7% absolute precision, and 10% nonresponse, the total sample size was calculated to be 216.

Statistical analysis

Data entry was done on Microsoft Excel spreadsheet. Tables were made to illustrate the results. Bar diagrams, pie charts, simple tables, and cross tables were made. In data analysis, for qualitative data, and proportions were calculated. The mean score with CI was calculated for quantitative data. Test of the significance of differences between proportions and mean was calculated. Qualitative data were analyzed by Chi-square test/ Fischer's test and *t*-test was applied for quantitative data. A $P = 0.05$ was assumed statistically significant. Multinomial logistic regression analysis was also done.

Results

A total of 248 women aged 40–65 years were enrolled. Of these, 133 were premenopausal and 115 were postmenopausal. Based on the exclusion criteria, 28 women were excluded, of which 21 were premenopausal and 7 were postmenopausal. Hence, the final analysis was carried out on 220 women, of which premenopausal and postmenopausal groups comprised 112 and 108 women, respectively. The mean age of women in premenopausal and postmenopausal groups were 44.9 ± 2.9 and 53.4 ± 4.8, respectively ($P < 0.0001$) (Data not shown).

The overall prevalence of MS in the entire cohort was 42.3% with 33% in the premenopausal group and 51.85% in postmenopausal women, the difference being statistically significant ($P = 0.005$). Sociodemographic profile is compared between the women who had metabolic syndrome to those who were healthy [Table 1]. The mean age of women with and without MS was 49.34 ± 5.05 and 47.95 ± 5.61 just short of statistical significance ($P = 0.060$). A significant proportion (79.6%) of urban women was associated with MS as compared

Table 1: Sociodemographic profile of the recruited women

Components	Absent metabolic syndrome (*n*=127)	Present metabolic syndrome (*n*=93)	*P*
Age (mean±SD)	47.95±5.61	49.34±5.05	0.060
Education[a]			
Illiterate	30 (23.6)	31 (33.1)	0.211
Primary	28 (22)	12 (12.9)	
Secondary	47 (37)	32 (34.4)	
Senior secondary	22 (17.3)	18 (19.4)	
Occupation			
Homemaker	81 (63.8)	60 (64.5)	0.910
Working	46 (36.2)	33 (35.5)	
Parity			
P1	15 (11.8)	6 (6.5)	0.407
P2	42 (33.1)	32 (34.4)	
P3 and above	70 (55.1)	55 (59.1)	
Socio economic status[b]			
Upper	11 (8.7)	12 (12.9)	0.553
Upper middle	32 (25.2)	28 (30.1)	
Lower middle	55 (43.3)	34 (36.6)	
Upper lower	21 (16.5)	16 (17.2)	
Lower	8 (6.3)	3 (3.2)	
Residence			
Rural	42 (33.1)	19 (20.4)	0.039
Urban	85 (66.9)	74 (79.6)	
Body Mass Index			
Normal (18.5-22.9)	30 (23.6)	8 (8.6)	0.000
Overweight (23-24.9)	46 (36.2)	19 (20.4)	
Obese (≥25)	51 (40.2)	66 (71)	
Physical activity[c]			
Low	74 (58.3)	63 (67.7)	0.054
Moderate	43 (33.9)	29 (31.2)	
Vigorous	10 (7.9)	1 (1.1)	
Menopausal status			
Premenopausal	75 (59.05)	37 (39.78)	0.005
Postmenopausal	52 (40.94)	56 (60.21)	

[a]According to InSCED,[12] [b]According to modified Kuppuswamy socioeconomic scale,[13] [c]IPAQ-S.[14] SD: Standard deviation, InSCED: Indian Standard Classification of Education, IPAQ-S: International physical activity questionnaire (short version)

with a rural population (P = 0.039). The distribution of women differed significantly between the groups when BMI was considered (P < 0.05). Obese women (71%) and those with low physical activity (67.7%) were found in higher proportion in women with MS with significant association. The distribution of socioeconomic status (SES), parity, occupation, and education was comparable in both groups.

When the different components of MS were compared between the premenopausal and postmenopausal women, WC ≥80 cm was found in high prevalence in both groups of women [Table 2]. Both systolic and diastolic BP were raised and HDL level was decreased in postmenopausal women with statistical significance. Rest all other components were comparable. In multinomial logistic regression analysis [Table 3], postmenopausal status was found to be independently associated with MS when adjusted for age, education, occupation, physical activity, parity, SES, and residence (adjusted odds ratios [AOR]=14.77, 95% CI: 1.77–23.33, P = 0.013). The prevalence of MS increases with age, after adjusting for other sociodemographic factors (P = 0.000).

Postmenopausal women were categorized into four groups with regard to the number of years since menopause (<5, 5–9, 10–14, and ≥15 years). To explore the link between menopause according to number of years since menopause and the risk of MS, adjusted odds ratios (OR) with 95% CI of MS and its components for each quartile of duration since menopause is presented in Table 4 after adjustment for potential confounders, i.e., parity, education level, SES, occupation, physical activity, residence, and BMI. The risk of MS, abdominal obesity and high BP were highest in <5 year group and decreased thereafter. The risk for low HDL and high TG increased with the number of years since menopause, reaching the peak level in the 5–9-year group and then decreased while the risk of high fasting blood sugar increased reaching a peak in the 10–14 years' group. All the five components were present in a higher proportion in postmenopausal women (5.6%) as compared to premenopausal women (0.9%).

Discussion

The progression of normal aging characterized by reduction in sex steroid hormones as a result of gonadal failure has been associated with susceptibility to disorders in hormone-responsive tissues. Menopausal transition marked by substantial decline in estradiol levels with a subsequent surge in the circulating gonadotropins and androgen predominance have been linked to accelerated cardiovascular adverse events.[3]

Our study reveals that the overall prevalence of MS in the entire cohort was 42.3%, 33% being in premenopausal group and 51.85% in postmenopausal women with the most common component being abnormal WC in both the groups. All the components were proportionately higher in postmenopausal group and the mean range of their values was higher in postmenopausal group except TGs. Postmenopausal status was found to be independently associated with MS when adjusted for potential confounders. The risk of MS, abdominal obesity and high BP was highest in <5-year group and decreased thereafter. The risk for low HDL and high TG increased with the number of years since menopause, reaching the peak level in the 5–9-year group and then decreased while the risk of high fasting blood sugar increased reaching peak in the 10–14 years of group.

Table 2: Distribution and mean values of components of metabolic syndrome in pre- and post-menopausal women

Components	Premenopause (n=112)	Postmenopause (n=108)	P	OR (95% CI)
Obese (>25 kg/m^2)	53 (47.3)	65 (60.2)	0.056[a]	1.74 (1.02-2.97)
BMI (mean±SD)	25.62±2.99	26.18±3.43	0.198[b]	-
WC ≥80 cm	77 (68.8)	79 (73.1)	0.473[a]	1.25 (0.70-2.22)
WC (mean±SD)	85.99±11.22	86.87±11.58	0.568[b]	-
FBS ≥100 mg/dL	47 (41)	35 (43.5)	0.143[a]	0.67 (0.38-1.14)
FBS (mean±SD)	101.34±32.65	106.63±36.53	0.259[b]	-
TGL >150 mg/dL	30 (26.8)	31 (28.7)	0.751[a]	1.10 (0.62-1.98)
TGL (mean±SD)	131.23±30.75	127.90±34.82	0.453[b]	-
SBP ≥130 mmHg and/or DBP ≥85 mmHg	37 (33)	57 (52.8)	0.003[a]	2.26 (1.31-3.90)
SBP (mean±SD)	119.83±12.29	124.38±13.26	0.009[b]	-
DBP (mean±SD)	78.52±8.74	83.23±9.14	0.000[b]	-
HDL <50 mg/dL	65 (58)	78 (72.2)	0.027[a]	1.88 (1.07-3.30)
HDL (mean±SD)	45.12±8.71	42.91±9.14	0.068[b]	-

[a]Chi-square test used for comparison of proportion, [b]Student's t-test used for comparison of mean. BMI: Body mass index, WC: Waist circumference, TGL: Triglycerides, BP: Blood pressure, OR: Odds ratios, HDL: High-density lipoprotein, FBS: Fasting blood sugar, SBP: Systolic BP, DBP: Diastolic BP, SD: Standard deviation, CI: Confidence interval

Table 3: Multivariate logistic analysis to depict association of metabolic syndrome with menopausal status after adjusting for sociodemographic factors

Parameters	*P*	AOR	95% CI
MS	0.013	14.77	1.77-23.33
Age	0.000	2.51	1.89-3.34
Education			
Illiterate	0.260	2.93	0.45-9.06
Primary	0.706	1.44	0.21-7.65
Secondary	0.633	1.53	0.26-8.97
Senior secondary	1	1	1
Occupation			
Homemeaker	0.038	4.10	1.08-15.55
Working	1	1	1
Physical activity			
Low	0.06	13.97	4.53-22.75
Moderate	0.236	8.84	2.11-15.59
Vigorous	1	1	1
Parity			
P1	0.038	9.37	1.13-17.46
P2	0.307	1.94	0.54-7.00
P3 and above	1	1	1
SES			
Low	0.000	23.9	11.42-44.30
Upper lower	0.032	13.96	1.29-30.77
Lower middle	0.972	1.02	0.20-5.16
Upper middle	0.388	0.48	0.91-2.54
Upper	1	1	1
Residency			
Urban	0.442	1.70	0.43-6.61
Rural	1		1

MS: Metabolic syndrome, CI: Confidence interval, OR: Odds ratio, AOR: Adjusted OR

The strength of this study lies in robust statistical analysis to explore multidimensional interplays between various variables helping in reaching a meaningful conclusion, comparable demographic characteristics of the study population at par with published literature, and day-to-day clinical practice. Since the study is done in a public health-care facility that is accessible to and catering to a large population irrespective of their socio-economic status, it increases the external validity of the study. However, the study is not free of its limitations. Its major limitation is that being a cross-sectional study it cannot establish a direct causal relationship with the risk factors and it is merely a snapshot representation of the health status of the population in question at that point in time. The obvious nonincorporation of various familial and genetic factors, food habits, and daily average calorie intake might influence the study results. However, this study forms the premise for a future prospective robust study incorporating all these potential factors at a national level to explore further avenues in public health research.

In our study, we have found the overall prevalence of MS to be 42.3% which is comparable to the nationwide prevalence of 35% and other regional published literature.[5,6,15] Our study found a statistically significant difference between the prevalence of MS in the pre and postmenopausal group (33% vs. 51.85%, $P = 0.005$) and menopause was an independent predictor of MS in women. Menopause directly reduces the protective effect of ovarian hormones on various cardiovascular functions and indirectly influences various risk factors for coronary artery disease which is further compounded by its detrimental effect on glucose metabolism, body weight balance, and BP control. A larger reduction in estrogen, than androgens, along with increased levels of LDL cholesterol and reduced levels of HDL-C in postmenopausal women make them susceptible to MS.[16] All these factors act in unison to predispose postmenopausal women to develop MS. Postmenopausal women are more likely to be affected by MS. In a recent meta-analysis, it was reported that postmenopausal women are having 3.54 times the odds (2.74–5.03) of having MS when compared to their premenopausal counterparts.[16]

Women living in urban areas had a higher incidence of MS than rural areas similar to other studies.[17,18] Urban women with better socio-economic status have unhealthy lifestyle, more mental stress, inessential intake of salt, and red meat disproportionate to the amount of physical labor predisposing them to MS.[19] A recent study revealed that vigorous physical activities, when conducted at least 6 times per week, reduce the occurrence of MS significantly (OR 0.65, 95% CI: 0.45–0.94).[20]

There was higher proportion of obese women (BMI ≥25) who had MS as compared to normal and overweight individuals with significant difference ($P < 0.05$). The pathogenesis of obesity in the causal role of MS is associated with the generation of reactive oxygen species in excess of their elimination due to surge in the levels of free fatty acids in blood. This induces oxidative stress predisposing to insulin resistance. The other mechanism is assumed to be mediated by decrease in the activity of antioxidant enzymes and diminution of the antioxidant glutathione in the liver by high-fat diet. Subsequently, there is insulin resistance in muscle, liver, and adipose tissues that gives rise to pro-inflammatory cytokines and decline in anti-inflammatory cytokines propagating chronic inflammation.[21]

The most common component of MS in both pre- and post-menopause was abnormal WC (≥80 cm). Donato *et al.* documented 2.5 times risk of abdominal obesity in postmenopausal women compared to those who are

Table 4: Adjusted odds ratios with 95% confidence intervals of metabolic syndrome and its components for each quartile of duration since menopause after adjustment for parity, education level, socioeconomic status, occupation, physical activity, residency, and body mass index

	MS	WC	FBS	HDL	TG	BP
<5 years	7.41 (4.35-13.13)*	2.95 (0.36-23.82)	0.46 (0.04-4.81)	2.77 (0.25-33.33)	3.58 (0.38-8.26)	4.36 (0.43-13.44)*
5-9 years	1.67 (0.06-21.82)	1.16 (0.13-9.82)	0.59 (0.05-6.78)	5.26 (0.38 11.28)*	6.03 (0.58-16.08)*	2.96 (0.27-10.15)
10-14 years	0.74 (0.02-27.78)	1.09 (0.16-7.09)	1.62 (0.08-15.65)	2.22 (0.14-23.4)	1.15 (0.08-16.44)	2.77 (0.22-33.71)
≥15 years	1	1	1	1	1	1

*P<0.05. MS: Metabolic syndrome, WC: Waist circumference, TG: Triglyceride, BP: Blood pressure, FBS: Fasting blood sugar, HDL: High-density lipoprotein

menstruating.[22] However, we found that postmenopausal women have 1.25 times the risk of central obesity when compared to premenopausal women. A higher incidence of central obesity in individuals even with near normal or lower BMI has been recognized in the Asian Indian phenotype predisposing them to insulin resistance and cardiovascular adverse events when compared to Caucasians (C) of European ancestry. This predisposition is highly attributable to a relatively smaller built, the incidence of high insulin resistance, a relatively dysmetabolic adipocyte milieu found at a significantly lower BMI, and a higher proportion of abdominal fat deposition.[11] The entire cohort was above 40 years in our study and predisposition to abdominal obesity by virtue of racial susceptibility can be well accounted for the higher WC found in premenopausal women in our study when compared to other studies.[22,23] Furthermore, the role of estrogen in the possible regulation of appetite, energy intake, and expenditure as well as metabolism demonstrated in experimental animals may explain the postmenopausal disposition marked by hypoestrogenism toward obesity.[24] Hence, quite predictably, the majority of the studies including ours, reported from south-east Asia did not find any significant difference in WC in pre- and post-menopausal groups.[5,6] Although the mean age of women developing MS was higher (49.34 vs. 47.95 years), we could not reach statistical significance when these two groups were compared. This finding further reinforces the predisposition of women of this ethnicity to develop MS.

There was a significant rise in both systolic and diastolic BP in postmenopause (OR: 2.26, 95% CI - 1.31–3.90). Estrogen is assumed to have an effect on the arterial wall in maintaining its flexibility. Not counting this role, an altered estrogen to androgen ratio in postmenopause is presumed to affect the renin-angiotensin system causing BP changes. Apart from this postulated mechanism, obesity, elevated blood endothelin, and oxidative stress already discussed above are other probable causes of elevated BP in postmenopause.[25]

We found a significantly high incidence of low HDL (<50 mg/dl) in postmenopausal women which was validated by other studies.[26,27] However, Maria LF *et al.* in their cross-sectional study found HDL-C was higher (P < 0.001) in postmenopausal women by 11%. The rationale for this divergent finding was explained by authors as a mechanism of body to protect itself from the adverse effects of the biomarkers found during the menopausal transition with speculation for further research.[28] However, we considered it a variation of selection bias due to the inclusion of much younger women in the premenopausal group (26–49 years) whose average weight was higher than the postmenopausal group. A weight- and BMI-matched analysis will reveal the true picture for confirming such findings.

We discovered the highest risk of MS in postmenopausal women was during the first 5 years since menopause. Cho *et al*. also found the risk of abdominal obesity was highest during the first 5 years since menopause considering the changes of postmenopause occurring primarily in the early postmenopausal period.[29] We also speculate that the rapid changes in adiposity due to hormonal and metabolic changes immediately after menopause may contribute to increased risk of MS and abdominal obesity during this period. Our finding of declining glucose tolerance with age is a well-known concept. The reduction in glucose effectiveness and impaired insulin secretion in the second phase in old subjects account for the glucose intolerance in them.[30]

Conclusion

Our study shows that the prevalence of MS in postmenopausal women is significantly higher than in the premenopausal group. All the components were proportionately higher in postmenopausal group with a significant difference for high BP and Low HDL. Postmenopausal status was found to be independently associated with MS when adjusted for potential confounders. The risk of MS, abdominal obesity and high BP was highest in < 5-year-group and decreased thereafter while those for low HDL, high TG, and fasting blood sugar increased after 5 years of menopause. The fact that menopausal transition is one of the key factors that predispose women to MS gives

us an opportunity to intervene, screen, and treat women in the premenopausal period. With the possibility of reversal of MS with comprehensive general well-being check-ups and screening for various physical and mental health disorders, screening should start from an age well before menopause.

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Conflicts of interest

There are no conflicts of interest.

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