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ORIGINAL ARTICLE

# Study on Relation of Metabolic Syndrome with Menopause

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**Abstract** This study is carried out to determine the prevalence of metabolic syndrome (MS) in 148 women between 36 to 65 years using the International Diabetes Federation criteria in the North-Eastern part of India. The prevalence of MS and all its individual components were found to be significantly higher among postmenopausal as compared to premenopausal and perimenopausal women. Various components of MS except waist circumference shows a significant increase and homeostasis model assessment index for insulin resistance also showed significant differences between the three groups. All the MS diagnostic markers (except serum high density lipoprotein) showed a strong positive correlation with MS score among the groups. Further MS score correlated with indicators of insulin resistance evaluated. This study concluded that MS is highly prevalent among North-East Indian postmenopausal women seeking primary health care and its determinant factors related to age and sedentary habits. Thus recognizing and treating MS early with proper intervention can minimize complication.

**Keywords** Metabolic syndrome (MS) · International Diabetes Federation (IDF) criteria · Premenopausal women · Perimenopausal women · Postmenopausal women

## Introduction

The metabolic syndrome (MS) consists of a constellation of metabolic abnormalities and a significant health care problem in postmenopausal women which increases risk of cardiovascular disease [1, 2] and type 2 diabetes mellitus [3]. It is one of the main causes of death in postmenopausal women [4]. The prevalence of MS is high, 40–50 million people in United States are suffering from MS and most diabetics are insulin resistant [5]. Developing countries, particularly in south Asia are witnessing a rapid increase in type 2 diabetes mellitus and coronary heart disease [6, 7]. During the previous three decades, the prevalence of DM has doubled in India [8]. Insulin resistance and clustering of the MS components, frequently seen in South Asians, are important contributory factors [9]. Overall, the prevalence of the MS in Asian Indian women is 1.5–2 times higher as compared with men [10]. Though MS incidence is seen to rise among the postmenopausal women, there is a dearth of data on MS in relation to menopause from Indian subcontinent, especially from the North-East region. Rapid demographic, nutritional, and economic changes are occurring in Indians. Most importantly, globalization of diets and consumption of nontraditional fast foods have occurred at a rapid pace in urban areas [11]. Studies of MS on men and conclusions drawn from these studies may not be applicable to women [12]. Because the average life expectancy of women extends 20–30 years after menopause (one-third of the life span), the medical impacts of changes leading to MS on postmenopausal women are

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significant [13]. Therefore the objective of the present research is to determine the prevalence of the MS and its components in premenopausal, perimenopausal and postmenopausal North-East Indian women and their association with menopausal status.

## Materials and Methods

The present study is carried out at Gauhati Medical College and Hospital (GMCH), Guwahati, Assam, in the North-Eastern part of India. The study protocol was approved by the Research and Ethical Committee of GMC, Guwahati. Oral informed consent is obtained from the patients and their attendants prior to study. This cross sectional study is conducted in a group of 148 female subjects between age 36 and 65 years selected randomly from the outpatients Department of Endocrinology, Medicine and Cardiology, GMCH and also from the female attendants who accompanied them. The target subjects were divided into three groups according to their menstrual stage—premenopausal women ($n = 50$, age >35 years with a normal menstrual history), perimenopausal women ($n = 48$, age >40 years with less than 12 months of amenorrhea or changes in menstrual regularity) and postmenopausal women ($n = 50$, age >45 years with more than 12 months of amenorrhea).

In accordance with International Diabetes Federation (IDF) criteria for Asian Indians [14], MS is diagnosed in patients with three or more of the following symptoms:

- Abdominal obesity (waist circumference cutoffs)—women ≥80 cm (non-obligatory).
- Fasting glucose ≥100 mg/dl or known case of diabetes mellitus.
- Blood pressure ≥130/85 mmHg or known case of hypertension.
- Triglyceride ≥150 mg/dl.
- High density lipoprotein [HDL] cholesterol <50 mg/dl in women.

Few subjects were excluded from the current study. Females who were not fasting for at least 6 h, those who were on hormone therapy, pregnant or lactating females, premature menopausal females (<40 years), subjects with surgical menopause (e.g. hysterectomy), high blood pressure, increase blood glucose and females with history of any acute illness, alcohol consumption or smoking and subjects on medication (e.g. diuretic, sex steroids) which may interfere with the results of the present study were not included in the current study. Detailed anthropometric characteristics like body mass index, waist circumference, waist to hip ratio, systolic and diastolic blood pressure were recorded using detailed proforma. MS score is also calculated to evaluate the MS in individuals and the score increased progressively with increasing number of MS symptoms or components.

Taking all aseptic and antiseptic precautions, 5 ml of fasting blood were drawn from the median anticubital vein after 12–14 h of fasting and estimation of lipid profile (total cholesterol [15], triglyceride [16] and HDL [17] and serum fasting blood glucose [18] were done using double beam UV Spectrophotometer (Spectra scan UV 2600) and VLDL, low density lipoprotein (LDL) calculated using Friedwald's formula [19]. Estimation of serum fasting insulin [20] and serum follicle stimulating hormone (FSH) [21] were done using ELISA Microplate Reader (Biorad 680). Insulin resistance is estimated using homeostasis model assessment (HOMA-IR) from fasting serum glucose and fasting serum insulin using the oxford homeostasis model assessment calculator [22].

After the biochemical estimations, the results obtained were statistically analyzed by using statistical software Graph pad Instat version 3.36 and then prevalence of MS and its components were compared between different study groups by applying $\chi^2$ test. One way analysis of variance (ANOVA) is used to analyze differences in baseline characteristics between the groups. Correlations were observed by using linear regression analysis. The results were expressed as mean ± SD and were taken as significant when the probability ($p$ value) is less than 0.05 as percentage of the observing values of '$t$' at a particular degree of freedom.

## Results

Our results from Table 1 shows comparison between the anthropometric and biochemical characteristics among the three groups. Postmenopausal women has significantly higher mean systolic and diastolic blood pressure, waist circumference, waist to hip ratio, fasting plasma glucose, serum triglycerides, HDL cholesterol, serum insulin, HOMA index and FSH levels than premenopausal women. According to IDF definition, components of MS in menopausal transition, each component compared using the $\chi^2$ test is shown in Table 2 where hypertension (BP > 130/85 mmHg) is the most frequent diagnostic feature of MS among the groups followed by serum HDL Cholesterol and waist circumference. All the MS diagnostic markers (except serum HDL) showed a strong positive correlation with MS score in premenopausal, perimenopausal as well as postmenopausal women and the correlation is found to be statistically significant ($p < 0.05$) as shown in Table 3. This correlation coefficients ($r$) was obtained by linear regression analysis between the MS score and various parameters among the premenopausal, perimenopausal and postmenopausal women separately. A negative correlation is noted

**Table 1** Comparison of anthropometric and biochemical characteristics among the groups

| Parameters | #Premenopausal women ($n = 50$) | #Perimenopausal women ($n = 48$) | #Postmenopausal women ($n = 50$) | ANOVA #$p$ value |
|---|---|---|---|---|
| Age (years) | 39.72 ± 3.47 | 45.21 ± 2.40 | 56.82 ± 5.73 | <0.001 |
| Body mass index (kg/m$^2$) | 23.97 ± 4.06 | 25.77 ± 3.77 | 24.72 ± 4.10 | >0.05 |
| Waist circumference (cm) | 75.92 ± 8.26 | 79.43 ± 6.59 | 78.42 ± 7.40 | >0.05 |
| Waist to hip ratio | 0.82 ± 0.04 | 0.84 ± 0.05 | 0.85 ± 0.05 | <0.01 |
| Systolic BP (mmHg) | 124.84 ± 10.71 | 131.25 ± 9.85 | 144.16 ± 18.37 | <0.001 |
| Diastolic BP (mmHg) | 80.28 ± 8.45 | 86.81 ± 8.65 | 92.44 ± 10.70 | <0.001 |
| Fasting plasma glucose (mg/dl) | 91.76 ± 21.83 | 89.23 ± 17.26 | 113.16 ± 40.16 | <0.001 |
| Total cholesterol (mg/dl) | 175.42 ± 30.29 | 187.27 ± 26.44 | 176.04 ± 34.97 | >0.05 |
| Triglyceride (mg/dl) | 120.46 ± 31.85 | 121.71 ± 34.71 | 145.60 ± 36.87 | <0.001 |
| HDL-cholesterol (mg/dl) | 46.78 ± 11.13 | 48.17 ± 7.47 | 40.80 ± 10.56 | <0.001 |
| LDL-cholesterol (mg/dl) | 104.55 ± 27.97 | 114.76 ± 29.45 | 106.12 ± 32.52 | >0.05 |
| Insulin (μU/ml) | 14.30 ± 6.89 | 16.90 ± 6.10 | 19.61 ± 8.46 | <0.005 |
| HOMA-IR | 1.83 ± 0.89 | 2.15 ± 0.83 | 2.64 ± 1.22 | <0.001 |
| FSH (mIU/ml) | 7.64 ± 2.06 | 49.33 ± 18.09 | 74.61 ± 24.46 | <0.001 |

# Values are given as mean ± SD

*BP* blood pressure, *HDL* high density lipoprotein, *LDL* low density lipoprotein, *FSH* follicle stimulating hormone

# $p < 0.01$ highly significant, # $p < 0.05$ significant

between the MS score and HDL cholesterol in all the groups and weakest correlations were seen with FSH and MS score within the study groups. Age showed a positive correlation in premenopausal and postmenopausal women with increase of MS score. Moreover serum insulin levels and HOMA index also showed a strong positive correlation with MS score among the groups. Table 4 shows that the prevalence of MS increases significantly from premenopausal subjects to perimenopausal and postmenopausal subjects. Perimenopausal status increased the risk of MS by 6.429 times (2.17–19.08, 95 % confidence interval [CI] and $p < 0.001$) as compared to premenopausal status and the odds ratio for postmenopausal status is 7.667 (2.61–22.55, 95 % CI and $p < 0.001$) in comparison to premenopausal status. Figure 1 shows distribution of number of components (0–3 or more) of the MS. The premenopausal group has high number of subjects with less than three components of the MS ($p < 0.001$) whereas the number of women with more than three components increased in the perimenopausal and postmenopausal groups as compared with the premenopausal group ($p < 0.001$).

## Discussion

In the current study, the prevalence of MS is higher among postmenopausal as compared to premenopausal women. 10 % premenopausal, 41.67 % perimenopausal and 46 % of postmenopausal women according to IDF criteria were found to have MS. This finding is comparable to the findings of Pandey et al. [23] who found 55 % postmenopausal and 45 % premenopausal women to have MS according to IDF criteria. The prevalence of MS has greatly varied across different studies [24, 25]. Differences in socio-environmental and genetic factors, lifestyles, time since menopause and criteria used for defining MS could be some of the reasons for this variability.

The mean age, systolic and diastolic blood pressure and fasting insulin levels increased significantly in our study from premenopausal to perimenopausal status and continued to increase towards postmenopausal status. We have evaluated fasting insulin levels and calculated the well-established HOMA-IR which shows significant differences between the three groups.

But the waist circumference did not follow the same pattern and the mean values were found to be lower than shown by Heidari et al. [26] and Misra and Khurana [27]. No statistical significant difference was observed between the means in the three groups. At the same time we found that there is a strong correlation between waist circumference and MS score in all the three groups. Thus though waist circumference is undoubtedly an important determinant of MS, but there is a need for population-specific waist circumference cutoff point for defining abdominal obesity in women with MS in this part of the country, as compared to other studies. Probably, difference in genetic makeup

**Table 2** Comparison of prevalence of individual components of MS (according to IDF definition) in menopausal transition

| Components of MS | Prevalence in premenopausal women ($n = 50$) Frequency (%) | Prevalence in perimenopausal women ($n = 48$) Frequency (%) | Prevalence in postmenopausal women ($n = 50$) Frequency (%) | $^{\#}p$ value |
|---|---|---|---|---|
| WC $\geq$ 80 cm | 9 (18) | 15 (31.25) | 21 (42) | <0.05 |
| BP $\geq$ 130/85 mmHg | 12 (24) | 33 (68.75) | 29 (58) | <0.001 |
| FPG $\geq$ 100 mg/dl | 9 (18) | 17 (35.42) | 19 (38) | >0.05 |
| TGL $\geq$ 150 mg/dl | 15 (30) | 19 (39.58) | 29 (58) | <0.05 |
| HDL < 50 mg/dl | 15 (30) | 21 (43.75) | 31 (62) | <0.05 |

*WC* waist circumference, *FPG* fasting plasma glucose, *TGL* triacylglyceride, *HDL* high density lipoprotein, *BP* blood pressure

$^{\#}$ $p < 0.01$ highly significant, $^{\#}$ $p < 0.05$ significant

**Table 3** Correlation between MS score and various parameters

| | Premenopausal women | | Perimenopausal women | | Postmenopausal women | |
|---|---|---|---|---|---|---|
| | *r* value | $^{\#}p$ value | *r* value | $^{\#}p$ value | *r* value | $^{\#}p$ value |
| Age | 0.30 | <0.05 | 0.05 | >0.05 | 0.51 | <0.001 |
| BMI | 0.40 | <0.005 | 0.54 | <0.001 | 0.60 | <0.001 |
| WC | 0.47 | <0.001 | 0.67 | <0.001 | 0.66 | <0.001 |
| W–H ratio | 0.31 | <0.05 | 0.37 | <0.01 | 0.49 | <0.001 |
| Systolic BP | 0.47 | <0.001 | 0.62 | <0.001 | 0.65 | <0.001 |
| Diastolic BP | 0.49 | <0.001 | 0.60 | <0.001 | 0.56 | <0.001 |
| FPG | 0.29 | <0.05 | 0.31 | <0.05 | 0.44 | <0.01 |
| Total cholesterol | 0.37 | <0.01 | 0.63 | <0.001 | 0.61 | <0.001 |
| Triglyceride | 0.59 | <0.001 | 0.31 | <0.05 | 0.63 | <0.001 |
| HDL | −0.49 | <0.001 | −0.54 | <0.001 | −0.42 | <0.005 |
| LDL | 0.46 | <0.001 | 0.63 | <0.001 | 0.59 | <0.001 |
| Insulin | 0.58 | <0.001 | 0.36 | <0.05 | 0.26 | >0.05 |
| HOMA-IR | 0.61 | <0.001 | 0.40 | <0.005 | 0.33 | <0.05 |
| FSH | 0.27 | >0.05 | 0.24 | >0.05 | 0.10 | >0.05 |

*BMI* body mass index, *WC* waist circumference, *W–H ratio* waist to hip ratio, *BP* blood pressure, *FPG* fasting plasma glucose, *HDL* high density lipoprotein, *LDL* low density lipoprotein, *FSH* follicle stimulating hormone

$^{\#}$ $p < 0.01$ highly significant, $^{\#}$ $p < 0.05$ significant

**Table 4** Prevalence of MS according to their menopausal status

| Menopausal status | Total cases | MS present | | Odds ratio | 95 % Confidence interval | $^{\#}p$ value |
|---|---|---|---|---|---|---|
| | | Frequency | Percentage | | | |
| Premenopausal women | 50 | 5 | 10 | 1 | 2.166–19.080 | <0.001 |
| Perimenopausal women | 48 | 20 | 41.67 | 6.429 | | |
| Postmenopausal women | 50 | 23 | 46 | 7.667 | 2.607–22.546 | <0.001 |

$^{\#}$ $p < 0.01$ highly significant, $^{\#}$ $p < 0.05$ significant

and ethnicity may be the cause behind lower waist circumference cutoff in the south Asian population and specifically in the North-East Indian population. A need for setting lower cutoff points of waist circumference for Asian populations has been pointed out by several investigators. Molarius et al. [28] in his study have stressed that a substantial proportion of those who would need health advice would be missed according to the presently accepted waist circumference cutoff points and emphasized a need for population-specific waist circumference cutoff points. According to Misra et al. [29] cardiovascular risk seems to manifest at lower waist circumference level in

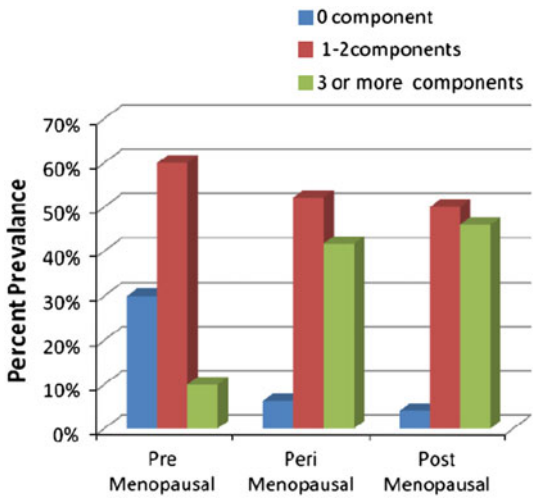


**Fig. 1** Distribution according to the prevalence of number of components of the MS (comparison using the $\chi^2$ test) in menopausal transition

Asian Indians as compared to Caucasians because Asian Indians have relatively higher truncal and abdominal fat mass as compared to Caucasians and black population despite similar or less average value of waist circumference [30, 31]. High body fat and truncal and abdominal adiposity may result in insulin resistance and other cardiovascular risk factors to manifest in Asian Indians with lower value of waist circumference than white Caucasians [31]. Thus the present study will encourage inquisitive minds for further detailed studies to define waist circumference cutoffs for MS in Asian Indians and further for the North-East Indian population.

Moreover the present study shows a significant difference in the prevalence of all MS components between the premenopausal, perimenopausal and postmenopausal groups except for fasting blood glucose as is seen in the study by Heidari et al. [26]. This finding suggests that high fasting blood glucose levels itself is not sufficient to diagnose MS. Rather fasting glucose levels may be within normal range in presence of insulin resistance.

The changing metabolic status and the pattern of fat substitution in different tissues with menopausal transition is one of the theories about the rising prevalence of MS in postmenopausal women. In premenopausal women, fat mainly gets deposited in lower extremities as a result of estrogen secretion. During menopause the pattern of hormone secretion changes. Estrogen secretion decreases and gradually causes many metabolic changes and fat accumulation in visceral tissues of abdomen resulting in central obesity [32]. However, it is controversial whether high premenopausal estrogen itself is protective or it only masks the genetic effect of MS incidence and resultant CVD. Again Janssen et al. [25] in his study stated that occurrence of MS in postmenopausal women was the result of testosterone hormone secretion.

MS is found to be highly prevalent among North-East Indian postmenopausal women seeking health care in GMCH. The major implications in causation of MS are changing hormonal milieu with declining estrogen and alteration of its ratio with testosterone. However, the contribution of other effective factors such as genetic or environmental influence on the different components of MS shows their effect in various ethnic groups differently.

Thus this study is undertaken to provide a better understanding of the MS and its different components in postmenopausal women in North-East Indian population and which may help in formulating the development of preventive primary and secondary strategies which would decrease the socioeconomic burden of the elevated rates of morbidity and mortality due to cardiovascular disease and diabetes.

Although a more elaborate study carried out on a larger population would have been more enterprising in establishing the actual relation between menopausal status and MS, but paucity of time, limited resource and the conduction of test in a single centre may be taken as limitation of our study. Endeavors must be made to screen the MS components in women from the earlier stages of menopausal transition in order to prevent the appearance of cardiovascular disease and type 2 diabetes mellitus. It is hoped that the present study will encourage new studies related to the above topic in a bigger way.

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