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Original Research Article

Association of metabolic syndrome and endometrial pathologies in postmenopausal women

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ABSTRACT

Background: The menopausal state may predispose the women to the development of metabolic syndrome as its prevalence has been reported to increase after the attainment of menopause. The aim of this study was to determine the prevalence of metabolic syndrome and its components in post-menopausal women and to assess the association between metabolic syndrome and endometrial pathologies in post-menopausal women.
Methods: An observational study conducted at gynecology OPD of GSVM Medical College, Kanpur and Total 80 post-menopausal women who had history of at least 1 year cessation of menses.
Results: Endometrial pathology was present in 63.2% of patients with metabolic syndrome and in 38.1% of patients without metabolic syndrome. The association between endometrial pathology and metabolic syndrome was found to be statistically significant (p=0.025). The highest incidence was found for fasting glucose (86.8%) followed by blood pressure (81.5%), high triglycerides (81%), low HDL (60.5%), and waist circumference (23.6%). Waist circumference, triglyceride, HDL, diabetes, waist circumference had postulated to be predictors for endometrial pathology.
Conclusions: Endometrial cancer is a type of metabolic syndrome-related tumor. Elucidating the specific roles and the possible mechanisms of metabolic syndrome in pathogenesis of endometrial cancer is expected to provide a new target for the early prevention and treatment of endometrial cancer.

Keywords: Menopausal women, Metabolic syndrome, Post-endometrial pathologies

INTRODUCTION

"Phases of menopause is not specific rather it is dynamic." World Health Organisation (WHO) defined "menopause as stoppage of periods for 12 months or stoppage of ovarian function leading to permanent amenorrhoea".[1] Menopause, a normal physiological process in women that often occurs at mean age of 50 years. Indian women attain menopause around the mean age of 48.7 year.[2] Metabolic syndrome (MetS) includes a combination of comorbid conditions central obesity, hyperlipidemia, high blood pressure, intolerance to glucose (type 2 diabetes and impaired glucose tolerance), and resistance to insulin. The menopausal state may predispose the women to the development of metabolic syndrome as its prevalence has been reported to increase after the attainment of menopause.[3] The relative importance of factors that influence cardiovascular risk in postmenopausal women are unknown. Alterations in lipid metabolism with estrogen deficiency are thought to be a substantial component of CVD risk in postmenopausal women, but there are also direct effects of estrogen deficiency on body fat distribution (central obesity), insulin action, the arterial wall, and fibrinolysis that may influence cardiovascular risk.[4] These factors contribute to an increased prevalence of the metabolic syndrome in postmenopausal women compared with premenopausal women, and this postmenopausal worsening of the metabolic profile may

contribute to the future risk of CVD.[5] The increased ageing and intolerance to glucose increases the morbidity of metabolic syndrome. The higher prevalence of metabolic syndrome in the postmenopausal women may be directly due to ovarian insufficiency and indirectly due to metabolic consequences of central fat redistribution with estrogen deficiency. Evidence has begun to link metabolic syndrome to certain types of cancer.[6] Recent reports have directly associated metabolic syndrome with endometrial cancer.[7] Further, other metabolic risk factors, such as hypertension and hyperglycemia, have also been associated with increased endometrial cancer risk, especially among overweight and obese women.[8,9] Endometrial cancer, one of the commonest cancers in women worldwide is strongly linked to lifestyle factors. Adult overweight/obesity is one of the strongest risk factors for endometrial cancer, accounting for approximately 40% of endometrial cancer incidence in developed countries.[7] As many as 60% of obese women suffer from related health problems including hypertension, insulin resistance, and dyslipidemia, which increases risk of endometrial cancer as well as other tumors and chronic diseases.[9] Overweight/obesity, diabetes, metabolic syndrome, nulliparity, late menopause and unopposed estrogen stimulation are established risk factors for endometrial cancer.[10] As there is a paucity of data regarding the prevalence of metabolic syndrome in Indian postmenopausal women hence we designed current study to find the prevalence of metabolic syndrome and its components and its correlation with endometrial pathology and metabolic syndrome.

METHODS

This prospective observational study was conducted in the department of obstetrics and gynecology, Upper India Sugar Exchange Maternity Hospital, GSVM Medical College, Kanpur, Uttar Pradesh, India. A total of 80 postmenopausal women who had undergone natural menopause defined by cessation of menstruation for ≥12 months were recruited for this study from 2019-2021.

Sample size

$$n \geq \frac{(Z_{1-\frac{\alpha}{2}} + Z_{\beta})^2 \times (\sigma_1^2 + \sigma_2^2)}{(\mu_{1-\mu_2})^2}$$

$Z_{1-\alpha/2}$= 1.96 for 95% confidence; Z_{β}= 0.84 for 80% power.

For preliminary estimates of μ_1, μ_2, σ_1, σ_2, results of the study of Ozdemier et al were used.[11]

The sample size came out to be n≥38.3 which was approximated to 40.

After inclusion criteria were fulfilled, written informed consent was taken from all women before recruitment for this study. Women on hormone replacement therapy, who were amenorrhoeic due to hysterectomy or cessation of periods other than by a natural cause, with history of renal impairment, hepatic impairment, history of smoking and alcoholism were excluded from the study. A detailed history with regard to age, race, and socioeconomic status, occupation, and drug intake, reproductive and personal profile were elicited. Menopausal rating scale (MRS) was used for the study participants to assess the symptoms of menopause.

Physical examination included the following parameters: 1) Body mass index (BMI): Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Those with BMI of 23.0-24.9 classified as overweight, while those with BMI>25 kg/m^2 defined as obese. 2) Waist circumference was measured at the point halfway between lower border of ribs and iliac crest in horizontal plane and hip circumference measured at widest level over greater trochanters. 3) Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured twice after 15 minutes of resting in sitting position in right arm. Repeat measurements was done at 5 minutes interval and average of 2 measurements taken.

Venous sampling was taken from all subjects and sent for fasting blood glucose, triglycerides, total cholesterol, low density lipoprotein cholesterol and high-density lipoprotein. After a complete history and physical examination, the patients were prepared for endometrial biopsy. Before the endometrial biopsy, transvaginal ultrasonography was performed to measure endometrial thickness. For endometrial aspiration, the endometrial cavity was curetted using Karman cannula and specimen was placed in formalin and sent for histopathological examination. Metabolic syndrome was diagnosed as per National Cholesterol Education Program Adult Treatment Panel III (ATP III) criteria. In order to make a diagnosis of the metabolic syndrome a patient must present with three or more of the following five risk factors:

Table 1: Metabolic syndrome: the NCEP ATP III definition.

Risk Factor	Defining Level
Abdominal obesity	Waist circumference
Men	>102 cm (>40 in)
Women	>88 cm (>35 in)
Triglycerides	≥150 mg/dl (1.7 mmol/l)
HDL cholesterol	
Men	<40 mg/dl (1.04 mmol/l)
Women	<50 mg/dl (1.29 mmol/l)
Blood pressure	≥130/≥85 mmHg
Fasting glucose	≥100 mg/dl (5.6 mmol/l)

Statistical analysis

Study data was analysed women in the groups were matched in regard to mean age, education, socioeconomic status and menopausal status. Values were expressed as mean±SD for continuous variables and number and

percentage for categorical variables. Odds ratio (OR) and its 95% confidence interval (CI) were calculated to estimate the relative effects factors and endometrial pathology. Multiple logistic regression analysis was performed.

RESULTS

In our study, the prevalence of metabolic syndrome was found to be 47.5%. Out of total 80 women, 38 women had metabolic. Out of 38 women with metabolic syndrome, 24 women were found endometrial pathology. Socio-demographic characteristics, menopause duration and biochemical parameters of this study population are described in Table 2. However, the menopausal patients who had metabolic syndrome had an average age of 61.6 years. Although there was no difference in age group between patients with and without metabolic syndrome, higher prevalence was noted around 61 years in menopausal patients. Patient with metabolic syndrome weigh heavier than the patients without metabolic syndrome (p=0.02). Though they did not differ in their height (p=0.342), there was a significant difference in their body mass index (p=0.03).

In our study when the components of MS were examined separately, fasting glucose was prevalent among 86.8% of women followed by systemic hypertension in 81%, hypertriglyceridemia in 81%, abnormal HDL (60.5%) and waist circumference in 23.6% as depicted in Figure 1.

As per histopathology report, 25% have atrophic endometrium, 8% endometrial adenocarcinoma, 12% proliferative phase, 20% simple hyperplasia (Figure 2).

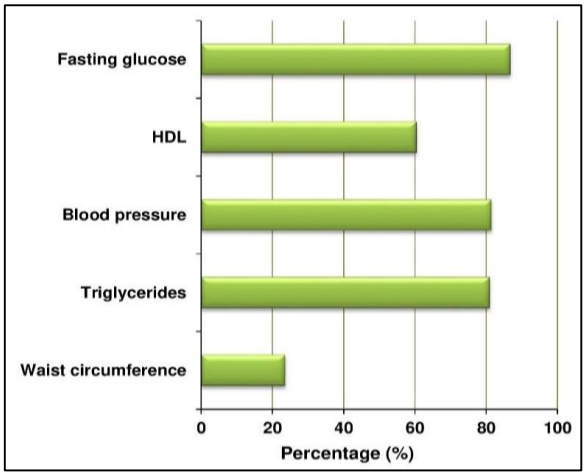

Figure 1: Different parameters of metabolic syndrome.

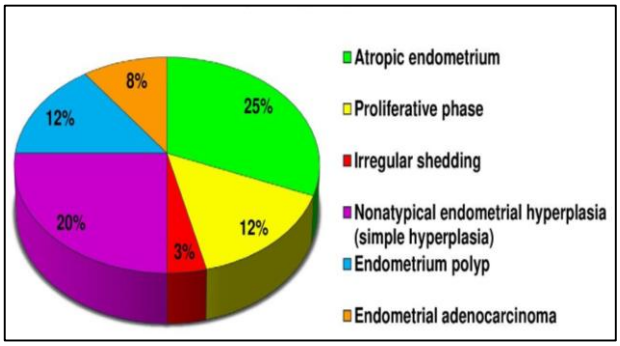

Figure 2: Distribution of cases with endometrial pathology.

Table 2: Demographic data.

Demographic data	Women with MetS (mean±SD)	Women without MetS (mean±SD)	P value	Women with endometrial pathology	Women without endometrial pathology	P value
Age (years)	61.1±6.8	58.1±8.1	0.40	58.4±4.3	55.1±4.2	0.16
Menopause duration	12.6±6.3	14±5.7	0.001	13±3.4	12±4.2	0.241
Socioeconomic status	12.6±9	14±7.7	0.2	13.3±9.8	13.3±7.4	0.58
Height	153±5.3	152±6.6	0.342	152±4.8	150±5.6	0.09
Weight	65.8±11.5	59.7±16.6	0.02	64.6±7.8	58±11	0.002
BMI	28.1±5.4	25.8±6.9	0.03	36.6±7.6	31.9±6.2	0.001

Table 3: Logistic regression analysis with endometrial pathology as dependent variable with metabolic syndrome as predictors.

				95% C.I. for O.R.	
Parameter		**Sig. ('p')**	**Odds ratio**	**Lower**	**Upper**
Metabolic syndrome	1.025	0.027	2.786	1.125	6.899
Constant	-0.539	0.109	0.583		

Table 4: Logistic regression analysis with metabolic syndrome as dependent variable and duration after menopause, waist circumference, BP, lipidimia and HDL, diabetes as predictors.

				95% CI for OR	
Parameters A		**Sig. ('p')**	**Odds ratio**	**Lower**	**Upper**
Menopause duration	-0.329	0.503	1.39	0.52	3.65
Waist	-1.574	0.205	4.8	0.42	55.6
BP systolic	-0.125	0.003	1.13	1.04	1.23
BP diastolic	-1.126	0.250	3.08	0.45	20.8
Triglyceride	5.220	<0.001	184.85	8.90	3838.37
HDL	3.353	0.001	28.599	3.677	222.43
Constant	15.867	0.007			
Parameters B					
Diabetes	2.373	<0.001	10.725	3.471	33.137
Constant	-0.724	0.017	0.485		

Table 5: Logistic regression analysis with endometrial pathology as dependent variable with waist circumference, lipid, HDL and diabetes as predictors.

				95% CI for OR	
Parameters		**Sig. ('p')**	**Odds ratio**	**Lower**	**Upper**
Waist circumference	0.371	0.615	1.449	0.342	6.134
Triglyceride	1.246	0.014	3.476	1.289	9.374
HDL	0.315	0.525	1.370	0.519	3.614
Diabetes	0.525	0.308	1.690	0.617	4.631
Constant	-1.244	0.096			

In this study, the regression coefficient for metabolic syndrome as predictor for endometrial pathology is statistically significant (p=0.027). The odds ratio >1, (OR=2.78) which indicate that endometrial pathology is at least 2.7 times more likely to occur in patient with metabolic syndrome (Table 3).

Table 4 depicted that relationship between metabolic syndrome and triglycerides level, systolic blood pressure and HDL was very strong. Among the various criteria triglycerides was found to have strongest positive correlation with the development of metabolic syndrome followed by HDL level and waist circumference. Triglyceride level had maximum relationship with an odds ratio of 184.85 (with 8.9 as the lower limit of 95% confidence interval. The OR in case of HDL was 28.5 (lower limit of 95% CI being 3.1 and BP systolic was 1.13 (lower limit of 95% CI being 1.04) respectively. Hypertension was not found to be strongly associated with metabolic syndrome. It was found that relationship between diabetes and metabolic syndrome is also statistically significant, the "odds ratio" for fasting plasma glucose is 10.72 with a 95% confidence interval of 3.5-33.1. This suggests that higher plasma glucose makes a woman at least 3.5 time more likely to develop metabolic syndrome.

In this study, waist circumference, triglyceride, HDL, diabetes had been postulated to be predictors of endometrial pathology. Out of them, an only triglyceride levels had statistically significant regression coefficient and we can safely infer that triglyceride is a significant predictor of development of endometrial pathology. The odds ratio was 3.47 with a lower limit of 95% CI being 1.289. This implies that in case of abnormal TG levels, the chance of developing endometrial pathology are at least 1.3 times more (Table 5).

DISCUSSION

The prevalence of metabolic syndrome using NCEP ATPIII criteria in our study population was 47.5%. A cross sectional study by Figueiredo et al done in Brazil on 323 women between 40 and 65 years of age showed the prevalence to be 44.4% in postmenopausal women and 24% in premenopausal women by NCEP criteria which was comparable to our results.[12] In a study done by Sharma et al from north India by NCEP ATPIII criteria, the prevalence of metabolic syndrome was found to be 65.7% in postmenopausal cohort.[13] The high prevalence was due to inclusion of all known hypertensive and known diabetics. The IDF criteria has been used by Pandey and colleagues in western India and documented the prevalence of metabolic syndrome to be 55%.[14] Though all studies for the prevalence of MS in menopausal women have shown a higher percentage of MS in postmenopausal as compared to premenopausal women, most have been cross-sectional. These differences in prevalence of metabolic syndrome in different studies could be attributed to different criteria used for defining MS, years since

menopause, the type of menopause (natural/surgical), socioeconomic and environmental differences, genetic factors and lifestyle.

In our study, the prevalence of various components of metabolic syndrome in the study population was also calculated. The highest incidence was found for fasting glucose (86.8%) followed by blood pressure (81.5%), high triglycerides (81%), low HDL (60.5%), and waist circumference (23.6%). Our study was partially in agreement with the study done by Gupta et al in which they found the maximum prevalent to be hypertension, followed by triglycerides, waist circumference and diabetes.[15] In a study done by Sawant et al in which abdominal obesity was found to be most prevalent factor followed by total cholesterol levels, fasting blood glucose, high triglycerides levels and low HDL levels in the decreasing order.[16] The overall higher prevalence of different components of metabolic syndrome in the various study can be explained by a possible significant effect of age group and the place of study chosen.

In our study, we tried to find the correlation between the different components of MS with the prevalence of MS. Maximum correlation of MS was found to be with triglycerides (OR=184.8), HDL (OR=28.5), diabetes (OR=10.7) followed by waist circumference (OR=4.8) and then hypertension. Sharma et al found the highest correlation between abnormal HDL level and MS and minimum correlation with hypertension and diabetes which was partly in contrast to our study while study carried out by Afzal and Bashir observed maximum correlation between hypertension and MS followed by obesity.[13,17]

In this study, we have also found the association between metabolic syndrome and endometrial pathologies. There was positive correlation between endometrial pathology and metabolic syndrome and was statistically significant (p=0.025). The odds ratio >1, (OR=2.78) indicate that endometrial pathology was at least 2.7 times more likely to occur in patients with metabolic syndrome. Similarly, Ozdemir et al study found positive correlation between metabolic syndrome and endometrial pathology with OR=5.53 and found a statistically significant (p<0.001) relationship between metabolic syndrome and endometrial pathology.[11]

Logistic regression analysis was used to estimate the multivariate ORs. ORs of endometrial pathology were 3.47 for triglycerides level, 1.69 for fasting blood glucose, 1.44 for waist circumference, 1.37 for HDL. Out of them triglyceride was a significant predictor of development of endometrial pathology. We observed that endometrial pathology was present in 64.4% women who had triglyceride level >150 mg/dl and the association between endometrial pathology and triglyceride levels were statistically significant. Lindemann et al studied the association of serum levels of triglycerides, total cholesterol, low-density lipoprotein cholesterol, non-high-density lipoprotein (non-HDL), and HDL cholesterol with endometrial cancer risk.[18] There was a positive correlation between serum triglycerides and BMI, R^2=0.11. Cust et al suggested that triglycerides was positively and HDL level was negatively associated with endometrial cancer risk, while total cholesterol and LDL were not.[19] One of the study done by Kaya et al observed that a fasting blood glucose level of higher than 110 mg/dl increased the risk of developing endometrial polyp and/or hyperplasia without atypia by almost five folds (OR:5.26, 95% CI:1.25-22.12), concluded that insulin resistance plays an important role in the development of benign endometrial pathologies.[20]

In summary, triglycerides, plasma glucose and hypertension have thus far been found to be the primary contributors to increased risk for endometrial cancer among the individual metabolic syndrome components. Although studies have suggested a relation between individual components of metabolic syndrome and endometrial pathologies, very little research has been conducted to determine whether metabolic syndrome better predicts endometrial pathologies risk than weight, diabetes, hypertension, dyslipidaemia, or dysglycemia alone. In this study, we were also able to examine criteria of metabolic syndrome that were all associated with an elevated endometrial pathology risk.

CONCLUSION

Although this study found strong association between metabolic syndrome and endometrial cancer, improving lifestyle is still the most important component in preventing the morbidity and mortality of endometrial pathologies. So, we should focus mainly on preventive measures along with pharmaceutical treatment wherever necessary. We should aim at reducing the underlying causes of metabolic syndrome such as obesity and physical inactivity while treating disease process such as dyslipidemia, hypertension, and cardiovascular problems. Further clinical studies are needed to investigate the therapeutic targeting of the metabolic microenvironment in metabolic syndrome-associated endometrial cancer.

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REFERENCES

1. WHO Technical Report Series 866. Research on the menopause in the 1990s. Available from: https://apps.who.int/iris/bitstream/handle/10665/41841/WHO_TRS_866.pdf?sequence=1. Accessed on 2 March 2023.
2. Burger HG, Dudley EC, Robertson DM, Dennerstein L. Hormonal changes in the menopause transition. Recent Prog Horm Res. 2002;57:257-75.

3. Petri Nahas EA, Padoani NP, Nahas-Neto J, Orsatti FL, Tardivo AP, Dias R. Metabolic syndrome and its associated risk factors in Brazilian postmenopausal women. Climacteric J Int Menopause Soc. 2009;12(5):431-8.
4. Kannel WB, Wilson PW. Risk factors that attenuate the female coronary disease advantage. Arch Intern Med. 1995;155:57-61.
5. Park YW, Zhu S, Palaniappan L, Heshka S, Carnethon MR, Heymsfield SB. The metabolic syndrome: prevalence and associated risk factor findings in the US population from the Third National Health and Nutrition Examination Survey, 1988-1994. Arch Intern Med. 2003;163:427-36.
6. Ford ES, Giles WH, Mokdad AH. Increasing prevalence of metabolic syndrome among US adults. Diabetes Care. 2004;27:2444-9.
7. Zhang Y, Liu Z, Yu X, Zhang X, Lü S, Chen X, et al. The association between metabolic abnormality and endometrial cancer: a large case control study in China. Gynecol Oncol. 2010;117:41-6.
8. Lindemann K, Vatten LJ, Ellstrom-Engh M, Eskild A. Body mass, diabetes and smoking and endometrial cancer risk: a follow up study. Br J Cancer. 2008;98:1582-5.
9. Faulds MH, Dahlman-Wright K. Metabolic diseases and cancer risk. Curr Opin Oncol. 2012;24(1):58-61.
10. Saad MF, Lillioja S, Nyomba BL, Castillo C, Ferraro R, De Gregorio M, et al. Racial differences in the relation between blood pressure and insulin resistance. N Engl J Med. 1991;324:733-9.
11. Özdemir S, Batmaz G, Ates S, Celik C, Incesu F, Peru C. Relation of metabolic syndrome with endometrial pathologies in patients with abnormal uterine bleeding. J Gynaecol Endocrinol. 2015;31(9):725-9.
12. Figueiredo Neto JA, Figuerêdo ED, Barbosa JB, Barbosa FD, Costa GR, Nina VJ, et al. Metabolic syndrome and menopause: cross-sectional study in gynecology clinic. Arq Bras Cardiol. 2007;95:339-45.
13. Sharma S, Aggarwal N, Joshi B, Suri V, Badada S. Prevalence of metabolic syndrome in pre- and post-menopausal women: a prospective study from apex institute of North India. J Midlife Health. 2016;7(4):169-74.
14. Pandey S, Srinivas M, Agashe S, Joshi J, Galvankar P, Prakasam CP, et al. Menopause and metabolic syndrome: A study of 498 urban women from western India. J Midlife Health. 2010;1(2):63-9.
15. Gupta R, Sarna M, Thanvi J, Rastogi P, Kaul V, Gupta VP. High prevalence of multiple coronary risk factors in Punjabi Bhatia community: Jaipur Heart Watch-3. Indian Heart J. 2004;56:646-52.
16. Sawant A, Mankeshwar R, Shah S, Raghavan R, Dhongde G, Raje H, et al. Prevalence of metabolic syndrome in urban India. Cholesterol. 2011;2011:920983.
17. Afzal S, Bashir MN. Prevalence of metabolic syndrome in pre and postmenopausal diabetics. Biomedica. 2008;24:26-30.
18. Lindemann K, Vatten LJ, Ellstrøm-Engh M, Eskild A. Serum lipids and endometrial cancer risk: results from the HUNT-II study. Int J Cancer Res. 2009;124:2938-41.
19. Cust AE, Kaaks R, Friedenreich C, Bonnet F, Laville M, Tjønneland A, et al. Metabolic syndrome, plasma lipid, lipoprotein and glucose levels, and endometrial cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC). Endocr-Relat Cancer. 2007;14(3):755-67.
20. Kaya S, Kaya B, Keskin HL, Kayhan Tetik B, Yavuz FA. Is there any relationship between benign endometrial pathologies and metabolic status? J Obstet Gynaecol. 2019;39(2):176-83.

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