

Assessment of Cardiovascular Risk Factors in Post-Menopausal Females

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Abstract

Introduction: Menopause is not a disease, but a physiologic phase of a woman's life, due to the changes of their hormonal status. Menopause is a physiological period of a woman's life during which she lacks menstruation continuously for 12 months. Lives have been extended with improved diagnosis and treatment modalities, and women spend 20-30 years in the post-menopausal period. Fastidious symptoms may be associated with changes in the metabolism together with new cardiovascular risk factors, particularly aggressive for the female cardiovascular system, unprepared because of the protection due to the fertile period. Changes of the lipid profile, obesity, hypertension, glucose intolerance and diabetes mellitus may intervene as severe risk factors. Cardiovascular disease represents therefore the most frequent cause of mortality and morbidity also in the female gender more than cancer. These changes are often ignored in Indian scenarios which are the important determinant of cardiovascular risk factors. Early diagnosis of these factors helps in early treatment and thus helps in a healthy ageing.

Objectives: Assessment of cardiovascular risk factor in Postmenopausal women.

Methods: Total 150 females were selected from general population with the age between 25-65 years. They were divided into two group namely premenopausal and postmenopausal women with each group having 75 subjects. 2D echocardiography was performed by standard methods. Blood sample was taken for Lipid profile and blood sugar in fasting state. Results were compared using student t test.

Results: Age and BMI shows significant difference in Postmenopausal women. Pulse & Blood Pressure profile shows a significant difference. IVSTd, IVSTs and PWT show significant difference in postmenopausal females. LVM and LVMI were statistically significant in Postmenopausal females. Fasting blood sugar, Serum Cholesterol, triglyceride, HDL and LDL shows statistically significant difference.

Conclusion: Potentially, adverse changes in LVM, LVMI, fasting blood sugar and lipid profile in postmenopausal women of the study group remark that this group of women is at increased risk of having complications associated with cardiovascular disease in near future. Early and timely detection and primary prevention can avoid morbidity and mortality in this high risk population. Early diagnosis of changes in postmenopausal women will help us to take

preventive measures early so as to reduce cardiac morbidity and mortality and to make healthy ageing.

Keywords: Cardiovascular Risk, Menopause, BMI, Echocardiography, Lipid Profile, Blood sugar.

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Introduction

Menopause is a permanent physiological state with cessation of menstruation attributable to the loss of ovarian function and reduction in the production of estrogen [1]. The average age of menopause is reported to be 51 years [2] but the age of natural menopause may vary from 40 to 58 years. It is a physiologic phase of a woman's life, due to the changes of their hormonal status. Menopause is not "per se" a disease, but can be a risk factor. Its onset may be accompanied by psychological and physical symptoms only, able nevertheless to influence quality of life of women. [3] Fastidious symptoms may be associated with changes in the metabolism together with new cardiovascular risk factors, particularly aggressive for the female cardiovascular system, unprepared because of the protection due to the fertile period. Quite all women moreover are affected by metabolic modifications which, sometimes, become a real cardiovascular risk profile, practically unknown through all the fertile life. The incidence of cardiovascular events in reproductive age women is 3 times lower than in men, whereas this ratio noticeably changes on menopausal beginning [4]. The high incidence of cardiovascular disease after menopause suggests a close association between hormonal level and cardiovascular system. [5] Cardiovascular disease (CVD) is one of the leading causes of death worldwide which is more prevalent in women after menopause. [6] This consists of a totally new risk profile, which intervenes rapidly without the so-called preconditioning phenomenon; this implies an aggressive influence on a unprepared organism. This metabolic high risk syndrome consists of hypertension,

dyslipidemia, obesity and insulin-resistance or frank diabetes. The risks related to postmenopausal women are mainly due to the abrupt interruption of estrogen, which has indirect protective effects on lipid & glucose metabolism and direct effects on vessel function. [7] Hence, present study is done to assess the risk factors focusing mainly on obesity, Blood Pressure, LVM & LVMI, Lipid Profile and blood Sugar Level.

Material and Methods

After obtaining the approval from the institutional ethical committee, 75 healthy premenopausal and 75 healthy postmenopausal subjects were selected for the study. A total of 150 Fasting blood sample was taken for the blood sugar & lipid profile. Blood sugar was done by GOD-POD Method. Total Cholesterol and HDL was done by CHOD-POD method. Serum Triglycerides was done by GPO-POD method. LDL cholesterol was assessed according to the formula $LDL = Total\ Cholesterol - (HDL + Triglycerides/5)$. It was done by the MINDRAY Auto Analyser. Cutoff points were as follows: Serum Triglyceride: >150 mg/dl, Total Cholesterol: >200 mg/dl, HDL: >45 mg/dl, LDL Cholesterol: > 130 mg/dl. Patient detailed history was recorded which includes demographic information; medical history, drug history and history of alcohol and smoking were taken. Anthropometric measurement such as height in meters and weights in kilogram were recorded. Body mass index was calculated using formula $BMI = Weight / (Height)^2$. Body Surface area was calculated using formula $BSA = 0.007184 \times (Height\ (m))^{0.725} \times$

$(\text{Weight}(\text{kg})^{0.425})$. Waist Hip Ratio was calculated.

After a resting period of 10 minutes, Pulse/min was recorded from radial artery and subsequently SBP (mm of Hg) & DBP (mm of Hg) was taken using well calibrated Diamond non mercury sphygmomanometer.

Subsequently, the study subjects were subjected for echocardiography which was done by a cardiologist for the Left Ventricular structural assessment by Siemen's ACCUSON Model no.KT-LM170SDS (Made in Germany) as per guidelines given by American Society of Echocardiography. Data was analyzed using Microsoft excel 2013.

Calculation: Left ventricular mass (LVM)= $0.8[1.04(\text{IVS}+\text{LVIDd}+\text{PWT})^3-(\text{LVIDd})^3+0.6$ (Devereux formula) 8 ; LVMi (indexed to BSA) = LVM/BSA ; LVMi (indexed to Height 2.7)= LVM/Ht

(m) 2.7 ; LVMi (indexed to Height) = LVM/Ht (m) 8

The obtained data were analyzed using Microsoft Excel 2010 and statistical software SPSS version 16. Results were compared using student t test. For these test P value of 0.05 or less is statistically significant.

Inclusion and Exclusion Criteria: Apparently healthy women between the ages of 25-65 years were included in the study.

Exclusion Criteria: The subject who had undergone hysterectomy, on hormonal replacement therapy, pregnant and lactating females, having irregular menses, diabetic females, CAD patients, respiratory disease, kidney disease, thyroid disease, hypertensive on treatment were excluded from the study.

Results:

Table 1: Demographic Profile

Demographic Profile			
Variables	Postmenopausal (n=75)	Premenopausal (n=75)	P-value
	Mean \pm SD	Mean \pm SD	
Age (Years)	54.00 \pm 4.78	33.18 \pm 6.02	<0.0001
Height (Meter)	1.6 \pm 0.07	1.62 \pm 0.08	0.10
Weight (Kg)	59.53 \pm 5.67	57.16 \pm 8.07	0.03
BMI	23.19 \pm 1.71	21.75 \pm 2.05	<0.0001
BSA	1.61 \pm 0.11	1.6 \pm 0.14	0.62
Waist Hip Ratio (WHR)	0.98 \pm 0.15	0.81 \pm 0.08	<0.0001

Table 2: Pulse & Blood Pressure

Pulse & Blood Pressure			
Variables	Postmenopausal (n=75)	Premenopausal (n=75)	P-value
	Mean \pm SD	Mean \pm SD	
Pulse (Beats/min)	78.17 \pm 4.67	76.40 \pm 3.41	<0.008
SBP (mm of Hg)	127.3 \pm 6.52	119.38 \pm 5.19	<0.0001
DBP (mm of Hg)	81.43 \pm 4.18	76.02 \pm 6.50	<0.0001
PP (mm of Hg)	47.75 \pm 4.05	46.18 \pm 4.53	<0.0001
MAP (mm of Hg)	94.52 \pm 4.71	91.53 \pm 5.71	<0.0001

Table 3: Echocardiographic Parameters

Echocardiographic Parameters			
Variables	Postmenopausal (n=75)	Premenopausal (n=75)	P- value
	Mean ± SD	Mean ± SD	
LVIDd (mm)	43.12±3.65	42.5±4.59	0.3
LVIDs (mm)	25.01±1.96	24.68±1.59	0.2
PWT (cm)	10.19±0.89	9.7±0.80	0.0005
IVSTd (mm)	10.44±0.97	9.94±0.67	0.003
IVSTs (mm)	11.92±1.44	11±1.09	<0.0001
LVM (gm)	157.32±25.55	108.09±11.08	<0.0001
LVMi (gm/m ^{2.7})	42.28±8.46	39.24±6.01	0.01
LVMi (gm/m ²)	124.19±11.29	90.21±10.50	<0.0001
LVMi (Ht)	96.48±11.59	93.21±8.84	0.05

Table 4: Blood Sugar & Lipid Profile

Blood Sugar & Lipid Profile			
Variables	Postmenopausal (n=75)	Premenopausal (n=75)	P- value
	Mean ± SD	Mean ± SD	
Blood Sugar (Fasting) (mg/dl)	102.13±6.67	86.79±8.37	<0.001
Serum Total Cholesterol (mg/dl)	184.24±18.65	132.84±17.44	<0.0001
Serum Triglyceride (mg/dl)	155.68±29.21	112.40±25.35	<0.0001
Serum LDL (mg/dl)	138.73±27.47	87.84±16.12	<0.0001
Serum HDL (mg/dl)	42.04±11.56	54.59±10.62	<0.0001
Serum VLDL (mg/dl)	23.17±7.64	21.82±5.04	0.20
LDL: HDL	3.29±0.8	1.60±0.58	<0.0001

Discussion:

Despite recent improvements in sex and gender research in cardiovascular disease (CVD), disparities still exist. Ischemic heart disease (IHD) in particular remains a leading cause of death in women. [9] The reasons for this are multifactorial and include biological, social, environmental, and economic factors. [10] While men and women share many traditional risk factors for CVD, these alone do not explain the sex-specific increased risk of CVD in women. Additional female-specific risk factors, most notably menopause, contribute significantly. Menopause has been associated with an increased CVD risk in women aged ≥ 55 years. [10] The transition to menopause has shown to be associated with negative alterations in the lipid profile, increased susceptibility to weight gain and metabolic syndrome, and

both epicardial and paracardial fat deposition. [11-12] The present study documented that Postmenopausal women have significant increase in BMI and WHR. WHR is used to indicate the abdominal fat accumulation and is more predictive than BMI. These are the indicators of obesity in postmenopausal women. Prevalence of obesity may be as high as 40% in postmenopausal women [13]. Estrogen promotes and maintains the fat distribution by enhancing the usage of lipids as energy source and promotes abdominal fat reduction. Hence, in postmenopausal women the decline in estrogen results into increase in the abdominal fat leading to increased WHR.

The blood pressure profiles of postmenopausal women are in Prehypertensive group (JNC-7) or elevated blood pressure according to the newer

guidelines of AHA or ACC 2017 [14]. Obesity may lead to elevation in BP which causes the BP of postmenopausal women in the prehypertensive group. Prehypertension is one of the cardiovascular risk factors which might explain the cardiovascular morbidity and mortality in postmenopausal women. The rise in systolic blood pressure with ageing is mainly caused by an increase in vascular stiffness of the great arteries in combination with atherosclerotic changes in the vessel wall. Systolic blood pressure rises more steeply in ageing women compared with men, and this may be related to the hormonal changes *per se* during menopause. [15,16] Sympathetic activity is higher in postmenopausal women than in age-matched men, especially in women who are overweight. [17,18] Sympathetic overactivity is associated with abdominal visceral fat which is strongly related to increased inflammatory markers and oxidative stress. Another important change around menopause is an increase in insulin resistance which causes unfavorable changes in blood pressure, lipid metabolism, bodyweight and the development of the metabolic syndrome. [19]

In the study conducted by Tapadar S et al both hypertension and risk of ischemic heart disease increased to 77% and 43% in the study group compared to control group 50% and 30% respectively after menopause [20]. In a study conducted by Chang CJ et al, significant correlation between age and general obesity, central obesity and cardiovascular disease risk factors were noted [21]. Menopause was an independent variable in relation to the changes of glycosylated HbA1c, total and LDL cholesterol levels and TG levels and atherogenic indices. Similarly, Yuka N. A. et al found in his study that biological risk factors for CHD i.e. Blood pressure, serum lipids, uric acids, blood glucose and HbA1c together with serum hepatic enzymes were significantly associated with

menopause [22]. Our study shows the similar results.

LVM and LVMI show significant difference in postmenopausal women. Increased LV mass has been proposed to be a compensatory response to elevated blood pressure. Elevated LVM is a well described independent risk factor for adverse CV events and is associated with development of depressed left ventricular (LV) systolic function which is a precursor of heart failure. In case of prehypertensives, it may be due to early stage of hyperdynamic circulation & LV wall stress. [23] Increased LV filling which was due to volume overload or elevated venous return, which was responsible for elevated SV but not disturbing normal systolic function. In the early stages of prehypertension, there occurs elevation of adrenergic tone typically characterized by hyperkinetic status. Among so-called target organ damage, left ventricular hypertrophy represents the most interesting one, also because the only sometimes really reversible. All randomized and observational studies agree about the issue that smaller left ventricular mass (LVM) less are the risk of stroke, heart failure and coronary events. [24]

Framingham [24] states that prehypertension is strongly associated with an increased risk of MI and CAD. According to Richard B. Devereux [25], Left-ventricular hypertrophy was three times more common among participants with hypertension and two times more common among those with pre-hypertension compared with normotensive individuals. The mortality rate has been shown to be 50% higher in the prehypertensive adult compared to normotensive counterparts.

In the present study, lipid profile and fasting blood sugar level in postmenopausal women were significantly altered as compared to premenopausal subjects. The incidence of cardiovascular disease after menopause may be partly caused by

changes in the plasma lipid levels that occur following the menopausal transition. The increased risk of CAD following menopause is mainly related to the endocrinal influences on lipid profile. Due to the change in the lipid pattern and loss of cardioprotective effect of estrogen, postmenopausal women are at increased risk of developing cardiovascular disease. Our result was quite similar to the study conducted by Ifueko (2013), in which TC, TAG, HDL-C, and LDL-C were increased significantly with “P” value < 0.001 in postmenopausal women than in premenopausal women [26]. Likewise, Shenoy and Vernekar (2015) also found significantly increased TC, TAG, and LDL-C but the HDL-C was not increased significantly in postmenopausal women in comparison to premenopausal women [27]. Similarly, a study done by Derby et al. (2009) showed a result of significant increase in TC and LDL-C while TAG was increased nonsignificantly and there was no changes in HDL-C in postmenopausal women when compared to premenopausal women [28]. Most studies showed significant increase in LDL cholesterol level supporting the present study, without any contradiction. This obvious result observed in all studies may represent the fact that estrogen has direct effect on LDL metabolism. The main reason for the absolute increase in LDL may be due to the decrease in estrogen that stimulated the synthesis of LDL receptor which directly causes reduction of LDL receptor after menopause [29].

Conclusion

CV risk in women increases at the time of menopause, likely related to a combination of aging and the menopausal transition. Proper CVD risk assessment is imperative for improving long term CVD outcomes, guiding risk reduction therapy and determining safety of MHT if needed. All traditional risk factors should be assessed as well as current lipid cholesterol levels, blood glucose levels, and blood pressure.

All women should receive education on ideal body weight, a plant-based heart healthy diet, and optimal exercise routines. Early and timely detection and primary prevention can avoid CV morbidity and mortality in this high risk population. Early diagnosis of these changes in postmenopausal women will help us to take preventive measures early and thus makes a healthy ageing.

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