Effects of menopause on lipid profile parameters and body mass index in postmenopausal women

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Abstract

Background: Coronary artery disease is the leading cause of morbidity and mortality in the present era. The incidence of this cardiovascular disease in women increases with age and after menopause. Postmenopausal rise in the risk of coronary artery disease has proven to be associated with dyslipidemia in many studies.

Aim: To assess the association of body mass index and lipid profile in perimenopausal and postmenopausal women.

Materials and Methods: 38 women of postmenopausal age (47 to 55 years) and 38 women of perimenopausal age (40 to 47 years) were included in the case-control study after obtaining written informed consent. Body mass index was measured and serum lipid levels were measured in a VITROS 5600 analyzer. Association between body mass index and lipid parameters was done using SPSS software version 20. $p<0.05$ was considered significant.

Results: The body mass index of the postmenopausal women was significantly higher compared to perimenopausal women. Total cholesterol, triglyceride, and HDL levels of postmenopausal women were significantly higher compared to perimenopausal women. There was a strong positive correlation between body mass index, total cholesterol, triglyceride and HDL cholesterol.

Conclusions: Ageing and decrease in female sex hormones increases the risk of coronary artery disease in postmenopausal women. This study throws light on the usefulness of assessing dyslipidemia and body mass index to identify high-risk women to enable early therapeutic intervention for coronary artery disease.

Keywords: Body Mass Index; Coronary artery disease; Menopause; Lipid profile; Obesity.

Introduction

In this era of information and technology, where knowledge is available at the fingertips, we find many women unaware of menopause and its effects. Menopause is a stage in a woman's life where she loses her capacity to reproduce because of the loss of ovarian follicle function. Gradual decline in estrogen levels occurs leading to an estrogen-deficient state[1-3]. Permanent cessation of menstrual cycles at least, for one year is termed Menopause. This stage is inevitable in the lives of all women, where their life undergoes a transition from the reproductive stage to the non-reproductive stage. Women face a lot of physiological and psychological changes during this period[4]. Menopause is preceded by the perimenopausal stage. This is the period before the final menstrual cycle, 3-5 years before the last menstrual cycle, where women experience erratic menstrual flow and cycles[4]. The mean age of menopause in India is estimated to be 46 years, which is lower than in Caucasians. Therefore the significant period in a woman's life is spent in the postmenopausal age[4].

The risk of noncommunicable diseases increases after menopause, as the protective function of female sex hormones will not be there. One such non-communicable disease is coronary artery disease (CAD). An increase in blood pressure, blood sugar, lipid levels, aging, weight gain, sedentary lifestyle, and habits like smoking and alcoholism are the major risk factors associated with CAD[3]. These risk factors are present in both men and women, but female-specific increase in CAD can be attributed to menopause. When discussing lipid profile alterations and CAD, postmenopausal women should be paid more attention[5]. Fluctuations in hormone levels in women after menopause such as low estrogen,

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increased luteinizing hormone (LH), and Follicle stimulating hormone (FSH) cause alterations in lipid metabolism and increase the risk of CAD[3,6]. Especially the hormone estrogen has cardioprotective action[5]. Many studies have shown that estrogen administration can have a positive impact on lipid parameters[5]. There is evidence from previous studies that hormone replacement therapy (HRT) has been useful in decreasing the incidence of CAD[5,7]. But not all women in India can afford HRT[1].

Body mass index (BMI) is a known determinant of dyslipidemia[2,3,8]. Many research articles in the past have proven that high BMI has a significant association with total cholesterol (TC) and LDL (Low density lipoprotein) levels. Increased levels of LDL have been shown as a risk factor for the development of CAD[1,2]. Previous studies have shown that menopause was associated with an increase in the atherosclerotic risk factors such as TC, triglyceride (TG), and LDL whereas HDL (High density lipoprotein) was decreased[9,10,3]. In a study by Tiwari et al researchers measured serum lipid levels in postmenopausal women and compared the results with women of reproductive age group concerning BMI in both groups. Alva et al study reported a positive correlation between serum TG and BMI, a negative correlation with HDL and BMI and no significant correlation with cholesterol, LDL and BMI. They also found a significant positive correlation between estradiol and BMI[11]. Ingale and Deshpande carried out a cross-sectional comparative study in menopausal women. The study showed increased BMI values and did not show any significant change as per the duration of menopause[2].

Korean study by Kim et al measured BMI, lipid profile and lipoprotein A in Premenopausal, Perimenopausal and Postmenopausal women. HDL levels were higher in postmenopausal women compared to premenopausal women. There was no difference in HDL between perimenopausal and postmenopausal women. LDL levels were increased in postmenopausal women. TC showed a stepwise increase from premenopausal to postmenopausal women. TG levels were lower in premenopausal women compared to perimenopausal and postmenopausal women. Lipoprotein (A) levels were reduced in perimenopausal women. BMI was higher in premenopausal and perimenopausal women than in postmenopausal women[12].

Reddy kilim and co-researcher studied lipid profile and estradiol concentration in pre and post-menopausal women. They found out that lipid profile was significantly elevated, HDL was significantly decreased and atherogenic index (cholesterol/HDL) was significantly increased in postmenopausal women. The concentration of estradiol showed a negative correlation with cholesterol, TG, and LDL[13].

Many studies in the past have proven that high BMI has a significant association with TC and LDL levels. Increased levels of LDL have been shown as a risk factor for the development of CAD[1,2]. Hence in this study, we have tried to determine the effects of menopause on body mass index and lipid parameters in Indian women.

Materials & Methods

Design, setting and sample

This case-control study was conducted in the Obstetrics and Gynecology outpatient department at a tertiary care Centre of Kanachur Institute of Medical Sciences, Mangalore, India. The Institutional Ethics Committee Approval was obtained before conducting the study. After obtaining informed written consent, 38 women of postmenopausal age, who did not have a menstrual cycle for more than 1 year, in the age group of 47 to 55 years were recruited as cases and 38 BMI-matched women of perimenopausal age in the age group of 40 to 47 years, were recruited as controls. A simple random technique was the sampling method used. The sample size was calculated by applying the formula: $n = 2[(Z_1-\alpha/_2 + Z_{1-\beta})^2 \sigma^2]/ [d^2]$, where $Z_1-\alpha/_2$= 1.96 for a 95% confidence interval, Power = 80%, d = 2.86, and standard deviation (SD) (σ) = 5.83, based on the study of Deshpande[9]. A sample size of 38 cases and 38 controls were obtained after calculation.

Women with a history of type 2 Diabetes Mellitus, thyroid disorders, known cardiovascular diseases, alcohol consumption, smoking history, surgical menopause, premature menopause (<40 years), subjects taking any drugs that affect serum lipids like statins, pregnant and lactating women were excluded from the study.

Measurement

A detailed history was collected which includes name, age, address, any medical illness, diet history, menstrual history, previous history, family history, personal history and treatment history. A systematic general, systemic and obstetric examination was done. Body mass index was measured by noting height in kilograms and weight in square meters and applying the formula weight/(height)^2. Cases and controls were matched according to BMI. Body mass index was grouped as in the table 1[14].

Collection of blood sample and analysis

Study participants were informed to come in 10-12 hours fasting state. 5 ml venous blood was collected under all aseptic precautions. Serum was separated and estimations were done on the same day. Serum Fasting blood sugar was estimated by Glucose oxidase

peroxidase method[15], TC was estimated by cholesterol oxidase peroxidase method[16], TG was estimated by an enzymatic method[17], HDL was estimated by the direct method[16]. LDL was calculated by Friedewald's formula: LDL (mg/dl) = TC - HDL - TG/5. All the tests were done in a VITROS 5600 dry chemistry analyzer, by microslide reflectance spectrophotometry method using kits supplied by Ortho Clinical Diagnostics.

Statistical Analysis

Analysis was done by SPSS software version 20. Values were expressed as mean ± SD. Comparison of values between cases and controls was done by using an independent sample t-test. Chi-square test was used to find an association between BMI and lipid parameters in both groups. p<0.05 was considered significant. Correlation between the parameters was done by Pearson's correlation.

Results

Table 1: Classification of participants based on BMI.

Nutritional status	BMI(Kg/m^2)
Underweight	< 18.5
Normal range	18.5 – 22.9
Overweight	23 – 24.9
Obese I	25 – 29.9
Obese II	> 30

Table 2: Comparison of age, height and weight in perimenopausal and postmenopausal women.

Study variables	Perimenopausal Women (n=38)	Postmenopausal women (n=38)	Test statistics	P value
Age (years)	44.11±2.458	52.39 ± 2.756	13.836	0.0001*
Height (cm)	156.55±6.757	158.24±8.135	0.982	0.329
Weight (kg)	63.21±5.194	71.16±5.824	6.278	0.0001*

*p value <0.05 considered to be statistically significant

Table 2 gives the baseline details such as age, height, and weight of study participants. The age and weight of the postmenopausal women were significantly higher compared to perimenopausal women (Table 2).

Table 3: Comparison of Body Mass Index in perimenopausal and postmenopausal women.

BMI		Perimenopausal Women (n=38)	Postmenopausal women (n=38)	Test statistics	P value
18.5-22.9	Normal range	1 (2.6)	2 (5.3)	6.994	0.030*
23-24.9	Overweight	2 (5.3)	10 (26.3)		
>25	Obese	35 (92.1)	26 (68.4)		

BMI, Body Mass Index. *p value <0.05 considered to be statistically significant.

Women in the Obese I and obese II categories had a BMI of more than 25 Kg/m^2. Table 3 Showed that the BMI of the postmenopausal women was significantly higher compared to perimenopausal women.

Table 4: Comparison of Serum Cholesterol and Triglyceride in perimenopausal and postmenopausal women.

Study variables	Premenopausal Women (n=38)	Postmenopausal women (n=38)	Test statistics	P value
Cholesterol (mg/dl)	174.24 ± 31.403	195.82 ± 43.590	2.476	0.008*
Triglyceride	138.84 ± 62.676	231.16 ± 83.965	5.431	0.0001*
HDL(mg/dl)	37.01 ± 3.281	29.26 ± 3.281	-9.930	0.0001*
LDL(mg/dl)	109.45 ± 27.09	120.31 ± 36.06	1.485	0.142
FBS(mg/dl)	90.184 ± 10.07	93.826 ± 13.517	1.331	0.187

HDL, High Density Lipoprotein; LDL, Low Density Lipoprotein; FBS, Fasting Blood Sugar. *p value <0.05 considered to be statistically significant.

The TC, TG, and HDL levels of the postmenopausal women were significantly higher than that of perimenopausal women (Table 4).

Table 5: Correlation of BMI with lipid parameters and FBS in postmenopausal women.

	BMI	Cholesterol	Triglyceride	HDL	LDL	FBS
BMI	1					
Cholesterol	0.096 (0.566)	1				
Triglyceride	0.217 (0.190)	0.563** (<0.001)	1			
HDL	-0.099 (0.555)	0.324* (0.047)	0.225 (0.175)	1		
LDL	0.024 (0.886)	0.917** (<0.001)	0.195 (0.242)	0.196 (0.239)	1	
FBS	0.005 (0.974)	0.707** (<0.001)	0.184 (0.268)	0.151 (0.365)	0.755** (<0.001)	1

BMI, Body Mass Index; HDL, High Density Lipoprotein; LDL, Low Density Lipoprotein; FBS, Fasting Blood Sugar. ** Correlation is significant at the 0.01 level (2-tailed). *Correlation is significant at the 0.05 level (2 tailed). # r (p value) is being reported.

BMI did not show any correlation with lipid parameters and fasting blood sugar (FBS) in postmenopausal (Table 5) and perimenopausal women (Table 6). However, when both postmenopausal and perimenopausal women were assessed together, BMI showed a significant positive correlation with cholesterol, TG, and HDL (Table 7).

Table 6: Correlation of BMI with lipid parameters and FBS in perimenopausal women.

	BMI	Cholesterol	Triglyceride	HDL	LDL	FBS
BMI	1					
Cholesterol	0.245 (0.139)	1				
Triglyceride	-0.056 (0.737)	0.403* (0.012)	1			
HDL	0.050 (0.766)	0.528** (<0.001)	0.136 (0.417)	1		
LDL	0.303 (0.064)	0.904** (<0.001)	-0.013 (0.937)	0.419** (0.009)	1	
FBS	0.277 (0.092)	-0.057 (0.733)	0.124 (0.457)	0.004 (0.980)	-0.124 (0.457)	1

BMI, Body Mass Index; HDL, High Density Lipoprotein; LDL, Low Density Lipoprotein; FBS, Fasting Blood Sugar. ** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2 tailed). # r (p value) is being reported.

Table 7: Correlation of BMI with lipid parameters and FBS in both groups.

	BMI	Cholesterol	Triglyceride	HDL	LDL	FBS
BMI	1					
Cholesterol	0.273* (0.017)	1				
Triglyceride	0.392** (<0.001)	0.560** (<0.001)	1			
HDL	-0.452** (<0.001)	0.046 (0.696)	-0.303** (0.008)	1		
LDL	0.193 (0.094)	0.911** (<0.001)	0.191 (0.099)	0.059 (0.613)	1	
FBS	0.166 (0.151)	0.460** (<0.001)	0.218 (0.059)	-0.061 (0.601)	0.454** (<0.001)	1

BMI, Body Mass Index; HDL, High Density Lipoprotein; LDL, Low Density Lipoprotein; FBS, Fasting Blood Sugar. ** Correlation is significant at the 0.01 level (2-tailed). * Correlation is significant at the 0.05 level (2 tailed). # r (p value) is being reported.

Discussion

Coronary artery disease is the leading cause of morbidity and mortality in this present era. The incidence of CAD in women increases with age and after menopause[3]. Several studies have been done in the recent past to show the effect of menopause on lipid parameters[2,3,11,18]. Menopause has proven to be associated with dyslipidemia by many researchers[14,19]. The present case-control study reported elevated levels of serum cholesterol and TG in postmenopausal women compared to perimenopausal women. This finding is consistent with many other studies[11,18,20]. The possible mechanism underlying these lipid alterations could be post-menopausal decrease in estrogen levels. Hormone estrogen regulates many metabolic pathways like lipid metabolism, coagulation pathway, and free radical scavenging and acts as anti-atherosclerotic. Estrogen levels decline after menopause and this explains the increased incidence of CAD in females[7,13]. However, a study of Igweh et al did not find any statistically significant difference in levels of TC in the postmenopausal group which is in contrast to our study[18]. However, the study of Igweh et al determined that estimating the risk of CAD, TC levels is not the key factor but the other lipid profile parameter like a decrease in cardioprotective cholesterol HDL plays an important role. Many studies showed significant differences in LDL levels in postmenopausal women which is in contrast to our study[1,3,8,13]. This can be explained as changes in LDL levels takes time to reflect in the lipid profile.

Body mass index (BMI) is due to increased lipids and visceral adiposity. Our study showed increased BMI in cases which was statistically significant. In postmenopausal women, we found a positive correlation between BMI and serum levels of TG, LDL, FBS and negative correlation between BMI and HDL. Similar findings were seen in other studies[1,2,9,11].

Increased levels of TG occur in postmenopausal women because of decreased estrogen. Estrogen has a major effect on LDL receptor metabolism. It helps in the clearance of LDL by hepatocytes to decrease LDL cholesterol. Some of the atherogenic particles like Chylomicron remnants and very low density lipoprotein (VLDL) are eliminated by hepatocytes under the influence of estrogen. It also increases the production of Apolipoprotein A and thus increases HDL[1,3]. Phases of the menstrual cycle do affect the lipid parameters. However, phases of menstruation in the perimenopausal women were not considered in this study. Additionally, estrogen levels were not measured in the present study. Further studies with larger sample size along with the measurement of estrogen and its association with BMI and lipid parametes are warrented.

Conclusion

Coronary artery disease risk increases in women after menopause. Aging and a decrease in female sex hormones are the main causes of this risk. Risk assessment should be done before and after menopause. Important risk factors like blood sugar levels and lipid parameters should be estimated frequently. This study sheds light on the importance of measurement of lipid parameters and BMI in postmenopausal women for early treatment as a precautionary measure to protect women from CAD. Appropriate counseling, guidance regarding diet and exercise, and hormone replacement therapy in dyslipidemic women can help prevent the risk of coronary artery disease.

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