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Dyslipidemia is the hallmark of the metabolic syndrome in postmenopausal women

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Abstract

The incidence of cardiovascular diseases (CVD) increases after menopause and may be due to changes in the plasma lipid-lipoprotein levels that occur following menopausal transition. Physiological estrogen withdrawal during menopause plays a major role in abnormal lipid metabolism such as elevated low-density lipoprotein concentration. The aim of this study was to determine the relationship between dyslipidemia and the causative factors of metabolic syndrome in postmenopausal women. In this cross-sectional study, 290 postmenopausal Sudanese women were included. Lipid profiles were measured by spectrophotometer, estrogen hormone determined by ELISA, insulin resistance determined by HOMA-2 calculator and lipid accumulation product was calculated by the following equation (waist circumference in cm X triglyceride concentration in mM). The results revealed that total cholesterol, triglycerides, low-density lipoprotein levels and very low-density lipoprotein levels were significantly higher in the postmenopausal women with metabolic syndrome (MS) in comparison to those without the MS. Elevated total cholesterol levels were seen in 51.7 %, elevated triglycerides were seen in 49.7% and elevated low-density lipoprotein levels were seen in 29.3% whereas reduced high density lipoprotein levels were seen in 16.89% of the postmenopausal women. Total cholesterol, triglycerides and very low-density lipoprotein values showed a significant positive correlation with insulin resistance and lipid accumulation and a significant negative correlation with the estrogen hormone level. In addition, high density lipoproteins showed a significant negative correlation with lipid accumulation levels.

Introduction

Dyslipidemia is a major risk factor cardiovascular disease (CVD) that represents the main cause of death among postmenopausal women **[1]**. High level of total cholesterol (TC), low-density lipoprotein (LDL) and triglycerides (TG) are seen frequently in postmenopausal women (PMW) **[2]**. Observational studies that were carried out to compare lipid profile in women showed a slight but significant reduction in the high density lipoprotein (HDL) as well as an increase in TG and LDL levels in postmenopausal women when compared to premenopausal women **[3]**. However, Kuller et al observed that the LDL concentrations remain constant in women during menopausal transition, in addition they documented that in postmenopausal women with very low blood

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estrogen level the HDL2 fraction and Apoprotein A-1 decreased significantly **[4]**. Dyslipidemia of MS occur secondary to enlargement of abdominal adipose tissue that increases the blood free fatty acids level which consequently leads to raised TG values, low HDL values and increased LDL values. Dyslipidemia in MS patients might occur as a direct consequence of a global metabolic effect of insulin resistance that is characterized by excessive production of very low density lipoprotein (VLDL) and increased catabolism of HDL particles **[5]**.

Materials and methods

This descriptive cross-sectional study was conducted in the Gadarif State, Sudan. The study was permitted by Ethical Committee of the Faculty of Medicine and Health Sciences, University of Gadarif (Reference number: DOP 4-2018). Informed consent was obtained from each participant.

Subjects

Two hundred and ninety postmenopausal women were included, whose ages ranged between 45 and 70 years. In this study menopause was diagnosed when a woman has not menstruated for at least one year.

Methodology

Fasting blood sample was collected. Lipid profile and fasting blood glucose were measured by using spectrophotometer kits (Biosystems S.A., Barcelona, Spain).

Estrogen hormone determined by using the ELISA estradiol E2 kit (Immunometrics (UK) Ltd., London, UK).

Waist circumference in centimetres (WC) measured by placing tape measure halfway between the bottom of lowest rib and the top of hip bones on light clothes. Blood pressure was measured by sphygmomanometer.

Lipid accumulation product (LAP): LAP calculation equation is based on a combination of WC and plasma TG level. Specific LAP for women = (WC [cm]−58) × (TG concentration [mM]). Insulin resistance determined by HOMA-2 calculator**.**

Metabolic syndrome was diagnosed by using updated diagnostic criteria adopted by National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATPIII) that defines the MS as three or more of five abnormalities

1. Waist circumference of > 35 inches (88 cm) for females.
2. Triglycerides level of > 150 mg/dl.
3. High density lipoprotein cholesterol of < 50 mg/dl in women.
4. Blood pressure of > or = 130/85 mmHg.
5. Fasting glucose of > or = 110 mg.

Dyslipidemia diagnosed by using updated diagnostic criteria adopted by NCEP-ATPIII that defined dyslipidemia as: TC> 200 mg/dl, LDL-C > 100 mg/dl and TG >150mg/dl.

Statistical analysis

Statistical analyses were performed by SPSS version 25 (IBM SPSS Inc., Chicago, IL, USA). Descriptive statistics was employed in this study, results presented as means ± standard deviations (Mean ± SD). Independent samples t-test was conducted to compare the relationship between dyslipidemia and MS. Pearson correlation was computed to estimate associations between the variables. P value less than 0.05 was considered significant.

Results

Results are presented in the **Table 1** showing that total cholesterol, TG, LDL and VLDL were significantly higher in the postmenopausal women with MS relative to the group without MS (p=0.000). HDL was significantly low in the postmenopausal women with MS (p=0.011).

Table 1: Comparison of lipid profile between PMW with and without MS

Lipid profile	PMW with MS (n= 149)	PMW without MS (n=141)	P value
TC (mg/dl)	208.75±50.22	183.79±44.65	0.000
TG (mg/dl)	209.49±85.12	125.54±51.19	0.000
HDL (mg/dl)	80.35±38.15	90.82±31.59	0.011
LDL (mg/dl)	87.48±40.87	69.47±37.20	0.000
VLDL (mg/dl)	41.20±17.83	25.06±10.50	0.000

Table 2 shows the prevalence of dyslipidemia among postmenopausal women. More than one-half of the subjects (n=150) had elevated TC levels (51.7%). Elevated TG levels were seen in 49.7% (n=144) of the subjects. Elevated LDL levels were seen in 29.3% (n=85) of the subjects. Reduced HDL levels were seen in 16.9% (n=49) of the subjects.

Table 2: Prevalence of dyslipidemia PMW women

Dyslipidemia	N=290	%
TC ≥200 mg/dl	150	51.7
TAG ≥150mg/dl	144	49.7
LDL ≥100 mg/dl	85	29.3
HDL ≤50mg/dl (F)	49	16.9

Table 3 shows that TC, TG and VLDL values positively correlated with insulin resistance and LAP; on the other hand negatively correlated with estrogen level. HDL significantly negatively correlated with LAP.

Table 3: Correlation of lipid profile with estrogen hormone level, insulin resistance (HOMA2-IR) and LAP in postmenopausal women

Parameters	Statistics (Pearson correlation)	Estrogen	HOMA2 -IR	LAP
TC	r	-0.271	0.227	0.242
	p (2 tailed)	0.000	0.000	0.000
TG	r	-0.342	0.336	0.870
	p (2 tailed)	0.000	0.000	0.000
HDL	r	-0.040	0.050	-0.170
	p (2 tailed)	0.496	0.396	0.004
LDL	r	-0.154	0.096	0.117
	p (2 tailed)	0.009	0.101	0.046
VLDL	r	-0.314	0.303	0.778
	p (2 tailed)	0.000	0.000	0.000

Discussion

Our study revealed that TC, TG, LDL and VLDL were significantly higher in the postmenopausal women with MS in comparison to those without the MS; this is in agreement with several previous studies **[6,7]**. HDL levels were significantly lower among postmenopausal women with MS which approved with findings reported by Adam et al **[8]**. In our study, the postmenopausal women had hyperlipidemia which contributes to development of MS in these women this is in agreement with the finding documented by Genest **[9]**.

Possible causes of dyslipidemia include visceral obesity and insulin resistance. Enlarged visceral adiposity causes adipose tissues hypertrophy which reduces fatty acid trapping, this increase the hepatic uptake of free fatty acid **[10]**, this leads to excessive production of TG, which in turn increase the secretion of VLDL in the liver **[11]**. Enlargement of visceral adiposity in postmenopausal women occurs mainly due to reduced endogenous estrogen. The state of hypoestrogenism that occur in postmenopausal women would contribute in the development of dyslipidemia most probably by redistribution of fats from periphery to the abdomen **[12]** and by reduction in the normal dyslipidemic effect of estrogen that include up-regulation of LDL receptors **[13]**. Among our study population, estrogen hormone significantly negatively correlated with the TC, TG, LDL and VLDL, indicating the major role played by hypoestrogenism for the development of dyslipidemia. In addition, LAP which represent enlarged adiposity, significantly positively correlated with TC, TG, LDL and VLDL, and negatively correlated with HDL. These findings directly explain the role of enlarged central adiposity in the development of dyslipidemia among postmenopausal women.

The state of insulin resistance that occurs in the postmenopausal women with MS regarded as a trigger factor for development of dyslipidemia. In the presence of insulin resistance the visceral adipocytes fail to respond to lipolytic effect of insulin, so that large amount of free fatty acids released into the hepatic cells leading to disproportionate production of TG and TG rich VLDLs **[14]** which consequently leads to increased production of apo-B — the major protein of LDL **[15]**. In the present study insulin resistance positively correlated with TC, TG and VLDL confirming the central role of insulin resistance state in the development of dyslipidemia and metabolic syndrome in our subjects.

Conclusion

Postmenopausal hyperlipidemia occurs as a direct consequence of metabolic syndrome due to state of hypoestrogenism that leads to enlargement of central adiposity and insulin resistance. It warrants management of these conditions which will prevent the development of CVD in postmenopausal women.

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