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A Comparative Study of Lipid Profile in Pre- and Post-Menopausal Women with and without Diabetes

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Abstract

Menopause and aging are associated with changes in circulating gonadal steroid hormones, insulin sensitivity, body composition, and also lifestyle and social coordinates. The physiological changes that occurs during menopause is a shift towards a more atherogenic lipid profile. After the cessation of menses, researchers have found an increase in plasma triglycerides (TG), total cholesterol (TC) and low-density lipoprotein (LDL). Lack of estrogen is an essential contributory factor in the derangement of lipid metabolism in post-menopausal women which is associated with increased cardiovascular risk. The deleterious impact of diabetes mellitus in cardiovascular morbidity and mortality is greater in postmenopausal women compared to men. Hence, in this study lipid profile were analysed in pre and postmenopausal women with and without Type 2 Diabetes. Total cholesterol, low-density lipoprotein and triglyceride were increased in postmenopausal women with and without diabetes. It is also observed in this study diabetes exacerbates the dyslipidaemia indicating increased cardiovascular risks in women with diabetes.

Keywords: Menopause, Diabetes, Lipid profile

INTRODUCTION:

Menopause refers to the time in a woman's life when she stops having a menstrual period and is no longer fertile (1). Twelve consecutive months of amenorrhea with no other cause were defined as post-menopause (2). Menopause typically occurs between

49 and 52 years of age (3, 4). One of the physiological changes that occurs during menopause is a shift towards a more atherogenic lipid profile (5, 6) . After the cessation of menses, researchers have found an increase in plasma triglycerides (TG), total cholesterol (TC) and low-density lipoprotein (LDL), especially the small and dense particles which are more pro-atherogenic (5,6,7,8). Menopause results in changes in metabolism of glucose and insulin, body fat distribution, coagulation, fibrinolysis, and vascular endothelial dysfunction (9) It has been proposed that estrogen exerts cardio-protective action among pre-menopausal women by maintaining high level of high-density lipoprotein cholesterol (HDL-C) and lowering the low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG) (10,11,12,13). Lack of estrogen is an essential contributory factor in the derangement of lipid metabolism in post-menopausal women which is associated with increased cardiovascular risk (14). Currently, post-menopausal women account for more than 30% of the female population at risk for CAD in India (15). Coronary artery disease (CAD) is the leading cause of death among the post-menopausal women. Post-menopausal women are 4-8 times more likely to die of CAD than of any other disease (16). Data from the Framingham study suggest that female CAD morbidity rates accelerate more quickly than do those of males after the age of 45 years(17) Multiple risk factors have been identified as contributory to the development of CAD. The deleterious impact of DM in cardiovascular morbidity and mortality is greater in women compared to men. In 2011, DM was responsible for 281,000 deaths in men and 317,000 in women, the majority from cardiovascular causes (18). Despite being a strong risk factor for both sexes, a greater impact in mortality from CAD is seen in women than in men(19) . Its presence almost eliminated the sex-related difference in cardiovascular morbidity and mortality, approximating the risk level of the diabetic woman to the non-diabetic men [CVD is a major issue for women's health most predominantly at older age. The increased mortality rates conferred by presence of DM are more prominent in the female sex. Obesity and impairment in glucose tolerance are frequent pathophysiological conditions that generate lipid-related cardiovascular risk in women following menopause. As chronic inflammatory states, these conditions contribute to lipoprotein remodelling, compromising its function. Meanwhile, reduced estrogen levels contribute to a decrease in insulin sensitivity and aggravate metabolic disturbances(20) . Therefore, postmenopausal obese type 2 diabetic individuals are prone to a combination of disorders that markedly increases the risk of dying from cardiovascular events (21,22).

MATERIALS AND METHODS

Number of study participants ---The postmenopausal women selected were those with a history of natural menopause, who had cessation of menstruation for a minimum of one year, and premenopausal women who were studied were those who had regular menstruation. In the present study the total number of participants were 92. The age group of pre-menopausal group of women was between 25 – 50 and for the post-menopausal women it is between 45 – 75 . The first group consisted of 37 premenopausal women without diabetes, and second group consisted of 15

premenopausal women with diabetes, third group had 15 postmenopausal women without diabetes and fourth group consisted of 25 postmenopausal women with diabetes.

Inclusion and exclusion criterion – diabetic and non-diabetic women in the study were selected depending on the exclusion criterion. Women with any type of hormonal abnormality, cardiac problems, pregnancy, hormonal therapy, heavy exercise and familial hypertriglyceridemia were excluded.

Sample collection – after an overnight fasting for 12 -14 hours, sample was collected from the subjects. About 5 ml of venous blood was drawn under aseptic precaution in a sterile plain vacutainer from selected subjects. Sample for glucose estimation was separately taken in fluoride, oxalate voile and remaining sample is collected into a plane voile.. Glucose is estimated in plasma and lipid profile is estimated in serum. As soon as the sample is collected, serum is separated and estimations were done on the same day.

Assay method –assay of samples for all the estimations was done using Erba-chem-5 plus2 semi-automated analyser . The quality control is checked using control sera of two levels, cholesterol total and HDL estimations were done by chod/pap enzymatic method (23,24), triglycerides by gpo/pap end point method (25) . Glucose was estimated by GOD/PAP method (26, 27)

LDL was calculated using the Friedewald formula (28)

LDL-C = TC − (HDL-C + TG/5)

VLDL was calculated using the formula:

VLDL-C = TG/5

Results were reported as mean + standard deviation (SD).The data were analysed by one-way ANOVA with Tukey-Kramer Post Hoc test using SPSS version 20 and p value of < 0.05 was taken as statistically significant at 95% confidence interval.

Ethics—the blood was collected after taking written/oral consent from the subjects. This project has been approved by the ethical committee of Shadan Institute of Medical Sciences.

RESULTS

Table 1 gives the number and age of subjects in study groups. Premenopausal women without diabetes group was with 37 number of subjects having 39.2 ± 6.6 mean ± standard deviation years of age and premenopausal women with diabetes group was with 15 subjects having 39.5 ± 5.7, Postmenopausal women without diabetes group was 15 number of subjects having 51.0 ± 7.7 mean ± standard deviation years of age and postmenopausal women with diabetes group was 58.8 ± 7.9. Overall, the subjects were from 29 to 75 years of age.

Table 1: Number and age of subjects in study groups

Study groups	No of Subjects	Age range (Mean ± SD)
Premenopausal women without diabetes	37	29 – 54 (39.2 ± 6.6)
Premenopausal women with diabetes	15	32 - 49 (39.5 ± 5.7)
Postmenopausal women without diabetes	15	45 - 62 (52.4 ± 5.8)
Postmenopausal women with diabetes	25	50 - 75 (58.8 ± 7.9)
Total number of subjects	92	29– 75*

*Minimum and Maximum years of age

Fasting Blood Glucose and serum Lipid profile in the study groups were shown in Table 2. The analysis of results by ANOVA indicated the statistically significant mean values for all the parameters except HDL. Fasting blood glucose levels were clearly showed an increased level in pre- and post-menopausal women with diabetes. Total cholesterol was significantly increased in premenopausal women with diabetes and postmenopausal women with or without diabetes when compared to premenopausal women without diabetes indicating diabetes and post menopause caused the increased

Table 2: Fasting Blood Glucose and serum Lipid profile in the study groups

Study groups	Fasting Blood Glucose	Total Cholesterol (TC)	Triglycerides (TG)	HDL	LDL	VLDL	TG/HDL	TC/HDL
Premenopausal women without diabetes	95.2 ± 14.1	159.6 ± 26.1	112.6 ± 36.1	38.9 ± 5.8	98.4 ± 19.7	22.5 ± 7.2	2.95 ± 1.06	4.12 ± 0.48
Premenopausal women with diabetes	151.7 ± 32.9*	191.2 ± 38.8*	137.1 ± 47.6	39.9 ± 4.8	123.9 ± 30.1*	27.4 ± 9.5	3.40 ± 0.88	4.77 ± 0.65*
Postmenopausal women without diabetes	92.3 ± 12.4$^{@}$	187.6 ± 30.6*	180.1 ± 57.0*$^{@}$	40.4 ± 5.0	114.7 ± 32.3	36.0 ± 11.4*$^{@}$	4.53 ± 1.53*$^{@}$	4.66 ± 0.63*
Postmenopausal women with diabetes	154.9 ± 61.4*$^{\#}$	207.6 ± 53.6*	178.6 ± 34.7*$^{@}$	39.6 ± 6.4	124.9 ± 46.1*	35.7 ± 6.9*$^{@}$	4.59 ± 0.93*$^{@}$	5.27 ± 1.17*$^{\#}$

Statistical analysis done by one-way ANOVA with Tukey-Kramer Post Hoc test
Values are Mean ± SD; Statistically significant = $p< 0.05$
*Statistically significant when compared to premenopausal women without diabetes; $^{@}$Statistically significant when compared to premenopausal women with diabetes; $^{\#}$Statistically significant when compared to postmenopausal women without diabetes

levels of Cholesterol. Triglyceride levels were increased in postmenopausal women with or without diabetes when compared to premenopausal women with or without diabetes. There was no statistically significant change in mean values of HDL levels of all study groups. LDL was increased in premenopausal women with diabetes and postmenopausal women with diabetes. Triglyceride to HDL ratio was significantly increased in postmenopausal women with or without diabetes when compared to premenopausal women with or without diabetes. Total cholesterol to HDL was significantly increased in premenopausal women with diabetes and postmenopausal women with or without diabetes when compared to premenopausal women without diabetes and it was also noted the increased ratio of Total cholesterol to HDL in postmenopausal women with diabetes when compared to postmenopausal women without diabetes.

DISCUSSION

The physiological changes that occurs during menopause, due to reduced oestrogens, were thought to shift towards a more atherogenic lipid profile (29,30). After the cessation of menses, researchers have found an increase in plasma triglycerides (TG), total cholesterol (TC) and low-density lipoprotein-cholesterol (LDL-C), especially the small and dense particles which are more pro-atherogenic (29,30,31,32)) . Diabetes is another contributory factor of dyslipidemia due to insulin resistance. Thus postmenopausal women with diabetes are at greater risk of cvd .Higher levels of glucose contribute to the elevation of cardiovascular risk of populations. Increasing prevalence rates of type 2 diabetes mellitus (DM) have been attributed to aging, modern lifestyle and obesity epidemic, which predisposes to several metabolic disturbances linked by the insulin resistance(33,34,35) .

In this study an increased levels of cholesterol were found in postmenopausal women with or without diabetes and premenopausal women with diabetes compared to premenopausal women without diabetes. The increased level of Cholesterol in premenopausal women with diabetes was equal to that of postmenopausal women without diabetes indicating insulin is equally important to keep cholesterol under control and oestrogens are additional effect in postmenopausal women with diabetes

LDL cholesterol was increased in premenopausal women with diabetes compared to premenopausal woman without diabetes. Similarly a diabetic postmenopausal woman has more LDL compared to a nondiabetic postmenopausal woman. There was no significant difference was seen between pre and postmenopausal women without diabetes. These results indicate the bigger role of insulin in LDL cholesterol metabolism making postmenopausal women more vulnerable for CVD due to high cholesterol and LDL in this group.

Triglycerides, a type of blood fat typically measured alongside cholesterol, are even more risky in women compared to men. VLDL concentrations are mainly dependent on triglycerides. Triglycerides and VLDL were significantly increased in post-menopausal women compared to premenopausal women irrespective of diabetic or

nondiabetic subjects making triglycerides and VLDL are independent risk factors due to reduced oestrogen in postmenopausal women.

An important component of the lipid profile is HDL-C concentration (36) . Clinical and epidemiological data have provided evidence of an inverse relationship between low concentration of HDL-C and an increased risk for CVD (37) . HDL particles not only mediate reverse cholesterol transport (RCT) but also exhibit anti-oxidant, anti-inflammatory, anti-thrombotic and vasodilatory activities (38,39, 40) . The changes in the concentration of HDL-C and HDL particles composition after menopause have been subject of controversy. While some authors state that there is a decrease of HDL-C in post-menopausal women (29,30,32) , others have reported no changes (41) or even an increase in HDL-C (42,43).

In this study HDL-C did not show any change among all the four groups of women studied indicating it may not be under the influence of oestrogens or insulin.

An increased serum triglyceride to high-density lipoprotein cholesterol (TG/HDL-C) ratio has been reported as an independent predictor for cardiovascular events in the general population (44) . In postmenopausal and more importantly in postmenopausal women with diabetes, it becomes much more important. Some studies have shown an increase in this ratio in postmenopausal women. In this study the TG/HDL-C ratio was significantly increased in postmenopausal women with and without diabetes groups (Group 3 & Group 4) compared to premenopausal women with and without diabetes groups (Group 1 & Group 2). Also no significant increase in this ratio is seen in postmenopausal women with diabetes compared to nondiabetic postmenopausal women.

Total cholesterol and HDL-C ratio has been considered as an atherogenic factor. In this study the TC/HDL-C ratio was significantly increased in premenopausal women with diabetes and postmenopausal women both with and witout diabetes compared to premenopausal women without diabetes. Also we found a significant increase in this ratio in postmenopausal women with diabetes compared to postmenopausal women without diabetes.

All the cardio protective mechanisms are lost in menopause thus postmenopausal women develop an increased risk for cardiovascular disease due to increase in Total cholesterol, LDL and triglyceride. It is also observed in this study diabetes exacerbates the cardiovascular risks in women with diabetes.

CONFLICT OF INTEREST

All authors declare that there is no conflict of interest existing.

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