

Original Article

LIPOPROTEIN ABNORMALITIES AND BODY MASS INDEX DIFFERENCES IN TYPE 2 DIABETIC POSTMENOPAUSAL WOMEN IN TERTIARY CARE HOSPITALS OF PESHAWAR

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Objective: To detect serum lipoprotein abnormalities and Body Mass Index differences in type 2 diabetic post menopausal women compared to controls

Material & Methods: This case control study was conducted at Tertiary care hospitals of Peshawar, that is Hayatabad Medical Complex, Khyber Teaching Hospital, and Lady Reading Hospital over a period of two years i.e., from July 2005 to July 2008. One hundred and fifty diagnosed diabetes type 2 post menopausal females compared with fifty non diabetic post menopausal healthy controls were included. Determination of glucose, total cholesterol, high density lipoprotein cholesterol were assessed by enzymatic lab technique (Elitech) using micro lab 200 (Merck), and low density lipoprotein cholesterol was determined by Friedewald formula.

Results: The results indicated highly significant difference between the biochemical indices of cases and controls which included elevated levels of LDL-C ($p=0.001$), reduced levels of HDL-C ($p=0.001$) and triglycerides (TG) above the target levels ($p=0.000$). Body Mass Index showed significant change in diabetic postmenopausal females as compared to controls. ($p<0.015$).

Conclusion: Dyslipidemias in post menopausal diabetic females are more prevalent. Lipoprotein abnormalities are a risk factor for cardiovascular diseases which becomes more prevalent with the loss of estrogens and the decrease in High density lipoprotein (HDL) cholesterol levels that occurs concurrently with menopause.

Keywords: Dyslipidemia, Type 2 Diabetes Mellitus and Menopause.

Introduction

Diabetes is recognized as the coronary heart disease risk equivalent condition. Dyslipidemia affects 70% to 97% of people with diabetes. It is characterized by a low level of High Density Lipoproteins (HDL), increased levels of Triglycerides and Low Density Lipoproteins (LDL-C) particles of altered composition.¹ An increase in the incidence of coronary heart disease risk has commonly been reported in post menopausal women.² This difference may be due to the deleterious effects of diabetes on lipids and blood pressure in women. In women, total and low density lipoprotein (LDL) cholesterol increase with age, and this increase is accelerated by menopause, whereas cardio-protective high density lipoprotein (HDL) decreases. These changes lead to increased rates of coronary heart disease, myocardial infarction and stroke in post-menopausal women.³ The largest health threat to women over age 50 is cardiovascular disease.⁴ UK Prospective Diabetes study, with the aim to compare fasting lipid among type-2 diabetes mellitus also showed that lipid concentration

increases with age, but reached the plateau at the age of 50.⁵ It is of paramount importance to bring increased awareness of heart disease in women through these studies, because almost 65% of deaths occur in those with no previous symptoms. Women are less likely to be diagnosed correctly, less likely to undergo the correct re-vascularization procedure, and less likely to survive a major cardiac event than men. Post-menopausal women exhibit a steady increase in the incidence of coronary heart disease with age.⁶ Its occurrence is rare before menopause, suggesting that the loss of endogenous estradiol plays an important preventive role in CHD. Age-adjusted risk of CHD in post-menopausal women is increased by two- to three fold, as compared to premenopausal women.⁷ Cholesterol, hyperlipidemia is an important risk factor in the development of CHD among women. The Framingham study demonstrated that the total cholesterol increased after menopause.⁸ Women during fertile age have a lower risk of cardiac events but this protection fades away after menopause. The response to therapy may also differ in women because of

and higher fat proportions.⁹

Material and Methods

Study Design:

This was case control study was conducted on post menopausal female's patients with type 2 diabetes mellitus and compared with normal healthy females of the same age group.

Sample Size:

A sample of 150 subjects was selected, 150 were diagnosed patients of type 2 diabetes and 50 were normal non-diabetic healthy individuals.

Place of Study:

The study was conducted at Physiology Department, Khyber Medical College Peshawar. Diabetic post menopausal female patients were selected from three tertiary care hospitals of Peshawar i.e. Khyber Teaching Hospital, Lady Reading Hospital and Hayatabad Medical Complex. Controls were selected from the general population of Peshawar.

Duration of Study:

Two years i.e., from July 2005 to July 2008.

Inclusion Criteria:

Diagnosed post menopausal female patients of type 2 diabetes between age of 50-60 years

Exclusion Criteria:

Patients using insulin, having previous history of angina, severe vascular disease, nephropathy or other life threatening diseases, and patients taking corticosteroids or any drugs affecting lipid profile or diabetic status were excluded from the study.

Control Group:

50 normal healthy females, randomly selected, between age of 40-50 years.

Method of Data Collection:

Participants of the study were divided into two groups that are diabetic post menopausal females and age comparable female controls. For laboratory purposes the facility of Pakistan Medical Research Council, Khyber Medical College was availed.

The subjects were selected after taking written consent and detailed history and examination according to:

1. Questionnaire Performa
2. Consent form.

Fasting blood sugar and lipid profile was done for all the participants of the study. Participants were asked to come to the laboratory after an overnight fasting for at least 6 to 12 hours. Fasting blood samples were collected for measurement of plasma glucose

and lipid profile. The 2HABF (two hours after breakfast) samples were collected for random blood sugar using standard assays. Determination of glucose, total cholesterol, high density lipoprotein cholesterol was done by enzymatic lab technique (Elitech) by micro lab 200 (Merck), and low density lipoprotein cholesterol was determined by Friedewald formula. The diagnosis of Diabetes Mellitus was based on the American Diabetes Association criteria for type 2 diabetes Mellitus (fasting plasma glucose level higher than 126 mg/dl and /or glucose level exceeding 200mg/dl at 2 hours in the 75g oral glucose tolerance test). Anthropometric measurements were made with the participants wearing light weight clothes and no shoes. BMI (Body Mass Index) was calculated for each study subject using the Quetelet's index: $BMI = \text{weight (in kg)} / \text{height in metres squared (m}^2\text{)}$. For Asians the normal body mass index is from 18.5-22.9 kg/m², Body mass index considered overweight from 23-24.9 kg/m² and obesity is considered when body mass index is >25 kg/m².

Blood pressure (mmHg) was measured after 5 minutes of rest in a seated position by mercury sphygmomanometer. The blood pressure was recorded from the upper extremity, and elbow was slightly flexed and placed at heart level. The disappearance of sound (phase V) was used for the diastolic blood pressure. Correct cuff and bladder sizes were used. Mean blood pressure was calculated as diastolic plus one third of pulse pressure where pulse pressure was taken as the systolic pressure minus diastolic pressure. Participants were considered to have hypertension if systolic blood pressure (SBP) was ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg or if they were taking antihypertensive medication.

Data Analysis

The data was analyzed using SPSS version 16. The mean \pm SD was computed for the comparison of results. The distribution of cases among various criteria was represented by their percentage. The comparison of mean between two groups was tested by Student's t test. The p-value of highly significance was taken as <0.00, moderately <0.01, marginally as <0.05.

Results

Participants of the study were divided into two groups i.e. diabetic post menopausal females and age comparable female controls. **Table1** illustrates that the mean ages of the diabetic and control groups respectively, were 53.1 and 51.4 years.

The systolic blood pressure and diastolic blood pressure were significantly higher in post menopausal diabetic females as compared to postmenopausal healthy females.

Body Mass Index shows significant change in diabetic postmenopausal females as compared to controls ($p < 0.015$). When lipid profile of healthy females was compared with diabetic females we observed significantly higher levels of TC, LDL-C and TG levels in diabetic females ($p < 0.009$, $p < 0.001$ and $p < 0.000$ respectively). A decreased level of high density lipoprotein cholesterol (HDL-C) was observed in type 2 diabetes post menopausal patients as compared to normotensive control subjects ($p < 0.001$).

Discussion

Several potential interacting factors may contribute to the acceleration of coronary heart disease risk in women with diabetes. These include a greater tendency to poor glycemic control, elevations in blood pressure and circulating lipids, and development of obesity.¹⁰ First and foremost, a

healthy lifestyle is the best preventive medicine, which favorably protects the heart and maintains a favorable lipoprotein profile. Lipid abnormalities may be the result of the unbalanced metabolic state of diabetes (i.e. hyperglycemia and insulin resistance) but still there is moderate diabetes-associated dyslipidemia with improved control of hyperglycemia.¹¹ In our study the patients with diabetes were dyslipidemic with high plasma triglyceride and low HDL cholesterol concentrations. Longitudinal epidemiology has pointed to the importance of raised plasma triglycerides and low HDL Cholesterol as a risk factor for coronary disease in diabetic subjects¹² and there is supportive evidence for aggressive management of lipid disorders in type 2 diabetes.¹³

Table-1: Clinical characteristics cases and controls

Variable	Controls n=50	Cases n=150
Age (years)	51.9±6.09	53.2±4.92
SBP (mmHg)	122.06±8.06	160.13±13.37
DBP (mmHg)	83.73±6.25	93.33±10.70

Table-2: Various study parameters in cases and controls

Parameters	Cases (n=150)	Control (n=50)	P-value
Body Mass Index (BMI)			
Abnormal	136 (90.7%)	38 (76%)	0.015
Normal	14 (9.3%)	12 (25%)	
Blood Sugar			
Fasting blood sugar	182.33	85.23	0.000
Random blood sugar	245.38	115.53	0.000
Total Cholesterol (TC)			
>200 (abnormal)	96 (64%)	18 (36%)	0.009
>150 (normal)	54 (36%)	32 (64%)	
Low density lipoprotein cholesterol (LDL-C)			
>150 (Abnormal)	84 (56%)	11 (22%)	0.001
<150 (Normal)	66 (44%)	39 (78%)	
High density lipoprotein cholesterol (HDL-C)			
< 40 (Abnormal)	47 (1.33%)	4 (8%)	0.001
>40 (Normal)	103 (68.7%)	46 (92%)	
Triglyceride (TG)			
>160 (Abnormal)	109 (72.7%)	19 (38%)	0.000
40-160 (Normal)	41 (27.3%)	31 (62%)	

Majority of our patients (72.2%) had hypertriglyceridaemia which is consistent with the studies.^{14,15}

A 14-year follow-up study of 1,405 postmenopausal women demonstrated that a triglycerides level greater than 4.5 mmol/L was associated with a more than three fold increase in the risk of coronary heart disease related mortality.¹⁶ Lipoprotein abnormalities are an independent risk factor for coronary heart disease and there is some evidence that lipoprotein abnormalities increases with age in women.¹⁷ Another study has shown that lipoprotein abnormalities was a significant risk factor for coronary artery disease in both pre- and postmenopausal women.¹⁸ Diabetes increases the risk of coronary heart disease threefold in women, and puts them at the same risk as men of the same age. Much of this excess risk is due to the excess in other coronary risk factors which occur in diabetics.¹⁹

More women than men develop hypertension as they get older and we know that control of hypertension reduces the risk of both stroke and heart disease. In our study the SBP and DBP were significantly higher in post menopausal diabetic females as compared to postmenopausal healthy females ($p < 0.0001$ and $p < 0.05$ respectively).

Hypertension is one of the major risk factors for the development of coronary heart disease. The incidence of hypertension increases with age and is higher in men than in women up to the age of about 50. Beyond middle age, however, blood pressure in women exceeds that in men. It has been suggested that menopause may potentiate the age-related increase in systolic pressure, perhaps as a result of reduced arterial compliance. Our study is in agreement with the study done by Staessen et al²⁰ who measured the blood pressure of 315 women and followed them up for a median of 5.2 years. Those women who were postmenopausal had a 4-5 mmHg higher systolic blood pressure than their pre- and peri menopausal counterparts, and also, while there was no change in systolic blood pressure in premeno-pausal women during follow-up, the systolic blood pressure increased by 4 mmHg in 5 years in the postmenopausal and premenopausal women. In a cross-sectional study, Weiss et al²¹ found that postmenopausal women had significantly higher serum cholesterol compared to premenopausal women. In the Framingham Study²² women between the ages of 29 and 62 years who were followed-up in a longitudinal study for 18 years demonstrated a significant rise in serum cholesterol

levels between premenopausal and postmenopausal examinations, with the rise taking place within a short time of the onset of the menopause, thus suggesting a causal effect.

Type 2 diabetes is becoming ever more common, right along with one of its root causes - obesity. Diabetes should be thought of as a disease of blood vessels as much as a disease of sugar metabolism, as it greatly increases cardiovascular risk. The risk of heart disease in women with diabetes is increased as much as 6-fold.²³ Hubert et al indicated that being overweight is a cardiovascular factor; this condition is usually associated with other risk factors rather than constituting an independent factor itself.²⁴

For aging women to maintain an independent lifestyle is more difficult; they are particularly more prone to inactivity and obesity. Obesity and sedentary life style are more common in post-menopausal women than in men of the same age; both are strong risk factors for heart disease and stroke.²⁵

In the Nurses' Health Study²⁶ body mass index was strongly associated with death due to CHD, with the risk of CHD over three times higher among women with a body mass index of 29 or higher. Much of this increased risk can be attributed to influences on blood pressure, glucose tolerance and lipid levels. However, the presence of diabetes seems to negate any cardio protection that a woman may have. The findings of the present study are in line with these findings.

As women tend to have heart attacks later in life than men, they often have other diseases that mask cardiac symptoms. Coronary heart disease is more often of the silent type in women. Thus, women with heart disease tend to be both under investigated and under treated when actually the female gender is strongly associated with increased risk for heart disease. The one-year post heart attack mortality risk is 41% in women compared to 27% for men. Similarly, in hospitals, mortality rate is 13% for women compared to 7% for men. Our study suggests that, at least in postmenopausal women with an elevated level of serum total cholesterol, one should proceed immediately to lipoprotein analysis for further risk assessment.

Conclusion

In conclusion, this study has highlighted that diabetic dyslipidemia in post menopausal females is more prevalent. Lipoprotein abnormalities are a risk factor for cardiovascular diseases which becomes more prevalent with the loss of estrogens and the decrease

In HDL cholesterol levels that occurs concurrently with menopause.

Non-pharmacological intervention should be targeted towards a low-salt, low-fat, high-fibre diet and increased physical activity. Efforts to educate the populace on diabetes, and awareness of heart disease in women including the delayed onset needs to be emphasized at different forum levels of

education/ seminar programs. Diabetic women must aggressively manage their risk factors if they are to live a longer, healthier life.

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Medical News

NOVEL PROTEASE INHIBITOR ACTIVE AGAINST HEPATITIS C

Genotype-1 HCV is the most prevalent and difficult-to-treat HCV subtypes. Standard care is with pegylated interferon alfa and ribavirin, but more than 50% of patients don't respond or relapse. Inhibition of the NS3/NS4A HCV protease has been shown to suppress viral replication, the team randomized 34 treatment-naive patients to monotherapy with placebo or BI201335 at 20 to 240 mg once-daily for 14 days. This was followed by 14 days of use along with pegylated interferon alfa/ribavirin. Active monotherapy induced a rapid, dose-dependent decrease in plasma HCV RNA from baseline in all patients. Subsequently, viral load breakthrough was common. Addition of pegylated interferon alfa/ribavirin led to continuous viral load reductions in most patients. A further 19 treatment-experienced patients also received combination treatment with 48 to 240 mg BI201335 for 28 days. Viral loads fell and breakthroughs were seen in only 3 of these patients. In light of these and other findings, the researchers conclude that the data support "the investigation of different treatment regimens testing doses from 120 mg to 480 mg daily in phase IIb trials."