NON HIGH DENSITY LIPOPROTEIN CHOLESTEROL IN TYPE 2 DIABETES MELLITUS

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Background: Dyslipidemia consisting of elevated triglyceride, decreased HDL, and low-density lipoproteins LDL particles of altered composition is an important cardiovascular disease (CVD) risk factor in individuals with type 2 diabetes mellitus. Measure of Non-HDL cholesterol might be a useful marker of this risk. Presuming the value of non-HDL cholesterol we intend to determine whether non-HDL cholesterol, a measure of total cholesterol minus HDL cholesterol is elevated in patients with type 2 diabetes mellitus. **Methods:** Study population comprised of 60 patients of type 2 diabetes mellitus (24 men, 36 women) from diabetic clinic Jinnah Postgraduate Medical Center Karachi. Each subject was interviewed, examined, and investigated for blood pressure measurements, body mass index, and fasting blood glucose. Blood sample was analyzed to determine serum total cholesterol and HDL cholesterol on auto analyzer after at least a 12-h overnight fast. **Results:** The level of non-HDL cholesterol was elevated significantly ($p<0.01$) in hypertensive patients of type 2 diabetes in contrast to normotensive patients of same disease, while HDL cholesterol shows significant decrease (29.46*±6.55) in hypertensive diabetics as compared to normotensive diabetics (34.43 ±9.44). **Conclusion:** Non–HDL cholesterol was elevated in type 2 diabetics who suffering from hypertension.

Keywords: Non-HDL cholesterol, Type2 diabetes mellitus

INTRODUCTION

Patients with diabetes mellitus have a markedly increased risk for macro vascular disease. A person with diabetes and no known cardiovascular disease (CVD) has the same risk as a person without diabetes who has already had a cardiovascular event.[1] Millions of people are affected by diabetes mellitus world wide.[2, 3]

In addition, or perhaps as part of this high risk for CVD, patents with diabetes and pre-diabetes often have a dyslipidemic feature of metabolic syndrome.[4] Classic diabetic dyslipidemia characterized by elevated triglycerides, decreased high density lipoprotein (HDL) cholesterol and low-density lipoproteins (LDL) particles of altered composition.[5]

Atherosclerosis is a multifaceted process involving interactions among immune, coagulation, hormonal, and vascular systems, and dyslipidemia is leading risk factor for atherosclerotic plaque formation and development of coronary heart disease (CHD) events.[6] Researchers concluded that most of the debilitating complication of diabetes can prevented or delayed by prospective treatment of hyperglycemia and cardiovascular risk factors.[7,8]

It has been recently suggested that Non-HDL cholesterol might be a useful marker and better predictor of CVD than LDL cholesterol in diabetic as well as non-diabetic individuals.[9] Non high density lipoprotein cholesterol reflects total cholesterol minus HDL cholesterol and encompasses all cholesterol present in potentially atherogenic lipoprotein particles (Very low-density lipoproteins [VLDL], intermediate density lipoprotein [IDL], low-density lipoproteins [LDL], lipoprotein[a]).[10]

Friedewald's equation is generally considered to be less accurate with increasing triglyceride levels and inapplicable at triglyceride concentration >400mg/dl. The advantages of using Non-HDL cholesterol as a screening tool include the fact that it requires measurement of only total cholesterol and HDL cholesterol both of which can be measured reasonably accurately in a non fasting sample, as opposed the LDL cholesterol measurement, which requires a fasting sample.[11]

Data are currently limited although a few studies have demonstrated association between elevated Non-HDL cholesterol and increased atherogenic risk.[12] As diabetes mellitus increases the risk of cardiac and peripheral vascular disease twofold to sevenfold. so, present study was carried out to evaluate the level of Non-HDL cholesterol in patients with type 2 diabetes mellitus.

MATERIAL AND METHODS

60 patients of type 2 diabetes mellitus; age ranged 40 to 65 years, having 8 to 12 years of duration of diabetes and a good record of glycemic control were selected for this study from diabetic clinic JPMC Karachi. Patients having history of ischemic heart disease, renal disease or suffering from acute illness

were excluded. Pregnant / lactating mothers were also excluded.

The base line examination consisted of personal interviews, physical examination, and laboratory tests. Participants were examined in the morning after at least a 12-h overnight fast. After informed consent, fasting blood samples were collected for measurement of plasma glucose and lipid profile using standard assays.

Anthropometric measurements were made with the participant wearing light weight clothes and no shoes. BMI was calculated as weight (in kilograms) / height (in meters) squared. Arterial blood pressure (mm Hg) was measured after 5 minutes of rest in a seated position by mercury sphygmomanometer. The arterial 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 arterial 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 mm of Hg or diastolic blood pressure (DBP) >/= 90 mm of Hg or if they were taking antihypertensive medication. The study subjects were grouped as follows:

Group A- normotensive but hyperlipedemic

Group B- hypertensive and hyperlipedemic

Laboratory investigations

1. Serum glucose: Enzymatic-colorimetric (GOD-PAP) method.
2. Glycated hemoglobin (HbAlc): Ion exchange colorimetric method.
3. Serum total cholesterol: CHOD-PAP method by using Merck kit.
4. HDL-cholesterol: Immuno FS link method

Statistical analysis

The data was analyzed on the computer statistical programme SPSS version10. The mean ±SD was also computed for the comparison of results. The distribution of cases among various criteria was represented by their percentage. The difference in percentage was compared by statistical test with Chi-square or Yates corrected Chi-square test. The comparison of mean between two groups was tested by Student's't' test. Results were considered statistically significant if P value is less than or equal to 0.05

RESULTS

The physical characteristics and anthropometric measures were presented in Table I. The difference between both groups was not found as they were carefully matched in physical criteria. However, the body mass index shows significant change in group B as compared to group A.

Table II illustrates blood pressure measurements and blood glucose levels in study participants. Systolic as well as diastolic blood pressure values were significantly higher in hypertensive (group B) patients in comparison to non-hypertensive one (group A).

Lipid profile and non-HDL cholesterol was depicted in Table III. The total cholesterol, non-HDL cholesterol, total/HDL cholesterol ratio were all significantly higher in patients with diabetes in whom hypertension was found than in those with no hypertension. A significant decline was observed in high density lipoprotein (HDL) cholesterol in hypertensive patients of type 2 diabetes as compared to normotensive diabetics.

Table-1: General characteristics of study subjects

Variable	Group 'A' (n=30)	Group 'B' (n=30)
Age (Years)	53.2 ± 4.92	51.9 ± 6.09
Sex (male/female)	12(40%):18(60%)	12(40%) 18(60%)
Body mass index (kg/m^2)	24.66±2.89	26.68*± 3.77

The values are expressed as mean SD.

Table-2: Comparison of systolic blood pressure, diastolic blood pressure, fasting blood glucose, glycated hemoglobin (HbAlc), levels among groups of patient.

Variable	Group 'A' (n=30)	Group 'B'(n=30)
SBP (mmHg)	122.06± 8.06	162.93± 13.37*
DBP (mmHg)	83.73± 6.25	93.33± 10.70*
FBG (mg/dl)	97.10± 9.27	99.33± 7.34
HbA_1C (%)	7.14± 0.33	7.02± 0.26

The values are expressed as mean ± SD. The number of observation and units are given in parenthesis.

Table-3: Comparison of total cholesterol, high-density lipoprotein cholesterol and Non- HDL cholesterol levels among groups of patients.

Variable	Group 'A'(n=30)	Group 'B'(n=30)
Total cholesterol (mg/dl)	172.17± 17.7	246.57± 18.43*
HDL-cholesterol (mg/dl)	34.43± 9.44	29.46± 6.55*
Non- HDL cholesterol	137.74± 20.7	217.11± 32.6*
Ratio of total / HDL cholesterol	5.0	8.3*

The values are expressed as mean ± SD The number of observation and units are given in parenthesis.

DISCUSSION

Patients with diabetes or hypertension tend to be dyslipidemic with high plasma triglyceride, low HDL cholesterol concentrations which are recognized risk factors for cardiovascular disease.[13,14] Although many factors play a role in the accelerated atherosclerosis observed in diabetes, lipoprotein abnormalities are key contributors. LDL, the main cholesterol bearing lipoprotein, is major determinant of atherosclerosis in patients with diabetes. Elevated VLDL is also associated with increase in pro-thrombotic and pro-coagulant factors. Because of many lipoprotein abnormalities in diabetes an easily measuring composite indicator may be useful to treat patients with diabetes.[15, 16]

The adult treatment panel III of national cholesterol education programme (NECP) emphasizes the need of for optimization of LDL cholesterol levels, but it has been recently recommended that non- HDL cholesterol may be a better predictor of CVD in diabetes.[17] There are several advantages to the non-HDL cholesterol measurements. First, it makes no assumption about the relationship between VLDL cholesterol and triglyceride in patients with diabetes. Second, non-HDL cholesterol includes an assessment of all lipoproteins that containing lipoproteins considered to be atherogenic, i.e. VLDL, IDL, LDL, and lipoprotein (a). Finally, non- HDL cholesterol has many practical advantages in a clinical setting, including the ability to be assessed in patients with triglyceride levels > 400 mg/dl and in patients who are not fasting.[18, 19]

Kannel WB assesses the utility of non-HDL cholesterol in diabetes mellitus.[20] In the systolic hypertension in the elderly programme (SHEP), non-HDL cholesterol and LDL cholesterol had similar prediction value with triglyceride level>400mg/dl. However, non-HDL cholesterol but not LDL cholesterol was an independent marker of CVD when triglycerides were included in model.[21] Our data was in agreement with few other studies and show that in both men and women with diabetes, non-HDL cholesterol was elevated in hypertensive individuals which is common co-morbidity in diabetes and major risk factor for CVD.[22]

Because diabetic patients are at high risk for CVD morbidity and mortality, adequate risk assessment and management is imperative. Within the realms of the standard lipid profile, non-HDL cholesterol appears to be the parameter correlating best with apo B, the most atherogenic lipoprotein.[23] The simple non-HDL cholesterol measurement, which can be conducted in the non-fasting state and can be determined regardless of triglyceride concentration as a target for lipid lowering therapy. The adult treatment panel III of NECP suggested a therapeutic goal for non-HDL cholesterol of 30mg/dl higher than the goal for LDL cholesterol; there fore, in patients with diabetes, the goal would be a non-HDL cholesterol target of <130mg/dl.

Though our findings of the utility of non-HDL cholesterol in patients with diabetes were of short scale but they were of particular intrest considering the dyslipidemia that is common in diabetes. Our analyses provide strong supportive evidence that non-HDL cholesterol may be particularly useful in treating patients with diabetes.

CONCLUSION

Non-HDL cholesterol which incorporates all cholesterol in potentially atherogenic lipoprotein particles, VLDL, IDL, LDL cholesterol, and lipoprotein (a) was elevated in hypertensive patients with type 2 diabetes mellitus.

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