Research Article

Altered triglycerides and HDL-c are better marker for coronary heart disease in NIDDM

Suresh Santu Ugle*, Mahendra Dattatraya Bikkad

Department of Biochemistry, MIMSR Medical College, Latur 413512, Maharashtra, India

*Correspondence:
Dr. Suresh Santu Ugle,
E-mail: uglesuresh@rediffmail.com

ABSTRACT

Background: Abnormalities that characterizes lipoprotein metabolism in non insulin dependent diabetes mellitus (NIDDM) patients, fasting concentration of triglycerde rich lipoprotein especially very low density lipoprotein (VLDL) are higher, and those of HDL, commonly measured as HDL-c, are lower than among people without diabetes, which leads to increased triglyceride HDL-c ratio and insulin resistance. This type of diabetic dyslipidaemia is major cause of endothelial damage and thus coronary heart disease (CHD).

Methods: The study was carried at the Central Clinical Laboratory MIMSR Medical college Latur , NIDDM patient were selected after attending Medicine OPD MIMSR Medical college Latur, the lipid profile of 50 diabetic patients and 50 healthy subjects were determined and compared.

Results: In the control group I mean values of total cholesterol were 175.55 ± 29.87 mg %, LDL-c 110.60 ± 28.73 mg % , serum triglycerides were 108.39 ± 39.62 mg %,HDL-c were 44.45 ± 6.7 mg% and In the group II serum triglycerides 145.68 ± 68.94 mg% and were significantly increased as compared to group I. The serum HDL-c group II 41.46 ± 6.6 mg % were significantly decreased as compared to group I (P is <0.05).

Conclusions: A characteristic feature of NIDDM is the elevated triglycerides and lowered HDL-c levels, which leads to insulin resistance and CHD.

Keywords: NIDDM, Serum triglycerides, HDL-c, Insulin resistance and CHD

INTRODUCTION

The major independent risk factors for the development of atherosclerosis are the plasma cholesterol concentration, cigarate smoking, hypertension and diabetes, which are by them self's risk factor for coronary heart disease.[1] Despite recent decline in cardiovascular mortality, atherosclerotic disease is still major health problem facing Western society. Incidence of coronary heart disease has shown upward trends in Indian in last decade.[2,3] A large amount of epidemiological evidences also support the relationship between serum low density lipoprotein-cholesterol (LDL-c) and coronary artery disease (CAD) in Indians.[4] Serum high density lipoprotein-cholesterol (HDL-c) level have been found to have inverse relationship with the CAD.[5]

Diabetes mellitus is a common among Indians with CHD both in their land of origin and abroad.[6] Individuals with NIDDM are more likely to have multiple risk factors for CHD than age matched non diabetic subjects.

Peoples with diabetes have a risk of CHD two to five times that of nondiabetic individuals.[7-9] Abnormalities that characterizes lipoprotein metabolism in non insulin dependent diabetes mellitus (NIDDM) patients, fasting concentration of triglycerde rich lipoprotein especially very low density lipoprotein (VLDL) are higher, and those of HDL, commonly measured as HDL-c, are lower

than among people without diabetes.[10,11] NIDDM is an integral component of the metabolic syndrome.[12] In addition to triglycerides levels, overweight and plasma triglyceride to HDL-c ratio of three or greater as a reliable indicator of insulin resistance.[13] Infact Mc Laughlin & Colleagues[13] suggested that an elevated TG to HDL-c ratio may be "Clinically appealing marker because of it's robust association with Cardio vascular disease (CVD).[14] NIDDM is associated with increase in plasma triglyceride and decrease in plasma HDL-c concentration i.e. dyslipidaemia changes that have been identified as the increasing risk , of CHD. Since the classic risk factors do not account for the excess risk of atherosclerosis in NIDDM, we need new approaches to explain the connection of this risk factor and accelerated vascular disease. Thus the aim of our study was to investigate role of altered lipoprotein-triglyceride metabolism abnormalities in progression of CHD events in NIDDM.

METHODS

We studied 50 healthy and 50 diabetic patients matched for age and body mass index. Subjects were selected from medical, paramedical staff and general public who were around 40 to 60 year of age. All subjects were belonged to the Latur district of Marathwada region. Patient belonging to group II were selected after attending medicine OPD of MIMSR Medical College, Latur and diagnosed as diabetic. The healty subjectwere nonsmokers, nonobese, nonalcoholic and free from any disease and not taking any drugs that alter lipid and carbohydrates metabolism. All patients belonging to group II had NIDDM. Criteria of diagnosis of diabetic is: Fasting blood sugar levels not less than 140.0 mg % all subjects after taking informed consent was interrogated and detailed examination was done. Blood samples drawn after an overnight fast. After serum seperation the analysis was done on the same day. We estimated serum triglycerides by enzymatic method (Autopack Siemens kit) and total cholesterol by enzymatic methods (Autopack Siemens kit) HDL-c measured by phosphotungstate method (Autopack Siemens kit). LDL-c and VLDL-c values were calculated by Friedwald's equation.[15]

RESULTS

In the control group I mean values of total cholesterol were 175.55 ± 29.87 mg %, LDL-c 110.60 ± 28.73 mg %, serum triglycerides were 108.39 ± 39.62 mg %, HDL-c were 44.45 ± 6.7 mg% and In the group II serum triglycerides 145.68 ± 68.94 mg% and were significantly increased as compared to group I The serum HDL-c group II 41.46 ± 6.6 mg % were significantly decreased as compared to group I (P is <0.05).

Table 1: Serum cholesterol and other biochemical parameter in normal healthy subject (group I) and diabetic patient (group II).

| Variable	Group I	Group II
Total cholesterol (mg %)	175.55±29.87	•183.24±41.94
Triglycerides (mg %)	108.30±39.92	*145.68±68.94
HDL cholesterol (mg %)	44.45±6.70	*41.46±7.67
LDL cholesterol (mg %)	110.63±28.73	•111.77±35.37
VLDL cholesterol (mg %)	21.73±8.23	*29.16±13.77
LDL / HDL ratio	2.53±0.83	•2.79±1.06

N=50 in each group Comparison between group I and II • P is >0.05
* P is < 0.05

DISCUSSION

The catabolism of triglyceride-rich lipoproteins is initiated by lipoprotein lipase, an endothelial enzyme that hydrolyses the triglyceride moiety of chylomicrons and VLDL, and releases fatty acids for energy production in muscle and for storage in adipose tissue. The activity of this enzyme is generally lower in NIDDM patient than in non diabetic people of similar age and degree of adiposity: The difference is more striking for patient with both NIDDM and coronary artery disease (CAD).[16] Lipoprotein lipase activity is low in untreated or poorly controlled NIDDM and increase with improved glycaemic control.[17] In NIDDM passage of triglyceride-rich lipoproteins through the lipolytic cascade is delayed for two reasons: there is a shortage of catalytic sites on lipoprotein lipase, and overproduction of triglyceride saturates the sites that are available. Both mechanisms promote hypertriglyceridaemia. The two components of diabetic dyslipidaemia, high concentrations of triglyceride-rich lipoproteins and low concentrations of HDL, are closely interwoven. Hypertriglyceridaemia contributes to low HDL concentrations in one or combination of following reasons.[1] The first process involves the transfer of surface remnants'-redundant phospholipids and apolipoproteins from lipolysis of triglyceride – rich lipoproteins – to HDL particles. Because lipoprotein lipase activity is decreased and lipolysis impaired in NIDDM, there are fewer surface remnants available to be incorporated into the HDL particle.[2] The large amount of triglyceride-rich lipoproteins and their prolonged residence time in the circulation increased the exchange (mediated by cholesteryl-ester transfer protein) of esterified cholesterol from HDL to triglyceride-rich lipoproteins and of triglyceride to HDL particles. The result is enrichment of the HDL particle core with triglyceride. Enriched HDL has a faster catabolic rate than normal HDL which leads to a lower number of circulating HDL particles (Figure 1). Furthermore, the HDL particles in NIDDM are

smaller owing to a high hepatic lipase activity-another feature of NIDDM. Hepatic lipase has a great avidity for triglyceride-rich HDL and hydrolyses the triglyceride in the HDL core, which leads to a smaller HDL particle size. Small dense HDL and LDL particles are components of the dyslipidaemia of NIDDM.[18] The lipolytic process itself of Triglyceride enriched HDL may lower HDL particles number.
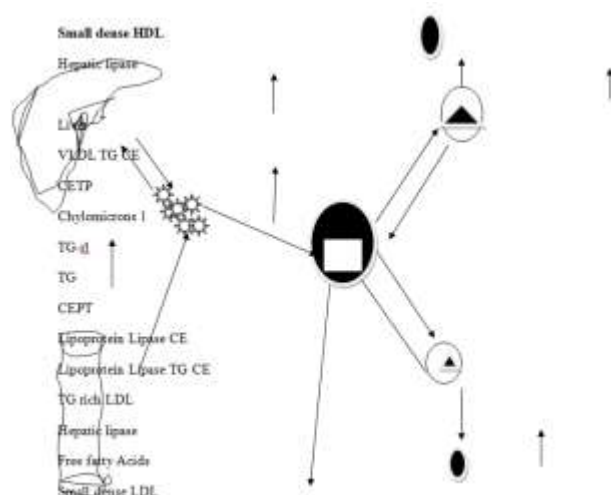
Figure 1: Increased production of VLDL by the liver and low lipoprotein lipase activity lead to raised concentration of triglycerides-rich (TG-rich) lipoprotein in plasma. High TG-rich lipoprotein concentration increase the transfer of TG to LDL and HDL and a concomitant transfer of cholesterol esters (CE) from LDL and HDL to TG-rich lipoproteins, all these reaction are mediated by cholesterol-esters transfer protein (CETP).

Lowered plasma HDL-c and elevated plasma triglyceride levels are features of NIDDM dyslipidaemia (TG/HDL-c ratio above 3) which is a reliable predictor of insulin resistance. Insulin resistance a syndrome that favours atheroselerosis and thus CAD. Relying on LDL-c or total cholesterol alone can be misleading. It is also proved that people with obesity, metabolic syndrome or diabetic lipid disorders often have raised triglycerides, low HDL-c and normal or closed to normal LDL-c.
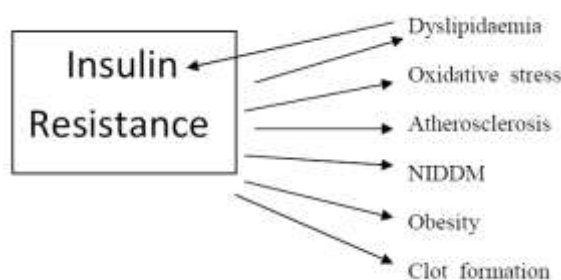
Figure 2: Biochemical and pathological consequences of insulin resistance.

In addition to this, insulin at physiological level has antiatherogenic effects in vasculature.[19] Many reports shows that in NIDDM activity of insulin to induce vasodilation is low due to insulin resistance.[20]

CONCLUSIONS

The lipid profile in NIDDM is abnormal, with hypertriglyceridaemia and low HDL-c concentration as the dominant features. This is because of insulin resistance or leads to insulin resistance and this disturb or impair lipoprotein metabolism. When the catabolism of TG- rich lipoproteins (chylomicrons and VLDL) is impaired, they become cholesterol enriched and possibly directly atherogenic and cholesterol rich lipoproteins become TG enriched.[21] The TG enriched HDL and LDL are atherogenic.[22] This atherogenic conditions needs to be a corrected before the development of end organ damage (Figure 2).

REFERENCES

1. Ross R. The pathogenesis of atherosclerosis: An update New Eng. J. Med. 1986314:488.
2. Dewan BD, Malhotra KC, Gupta SP. Epidemiological study of CHD in rural Community in Harayana. Indian Heart Journal. 1974;26:66-78.
3. Sarvothan SG, Berry JD. Prevalance of CHD in an Urban population in Northan India. Circulation. 1968;25:939-53.
4. Enas Ea, Garg A, Davidson MA. Coronary artery disease and It's risk factors in 1st generation immigrant Asian Indian to the United State of America. Indian heart J. 1996;48:343-53.
5. Castelli WP, Andreson KA. Population at risk prevalence high cholesterol level in hypertensive patients. Framingham study. Am. J. Med. 1986;80,(2A):23-28.
6. Bhoraskar AS, Raheja DS. Diabetes and cardiovascular disease Do Asian Indians have a high ethenic susceptibility. J.A.P.I. 1997;34:72-8.
7. World health organization (WHO). Prevention of Diabetes Mellitus in WHO Technical Report Series No 844. Geneva; WHO. 1994.
8. Panzram G. Mortality Survival in type 2 (non-insulin dependent) Diabetes mellitus. Diabetologia. 1987;30:123-31.

9. Meigs JB, Singer DE Sullivan LM. Metabolic control &Prevalent cardiovascular disease in non-insulin dependent diabetes mellitus (NIDDM); The NIDDM patient outcomes research group. Am J. Med. 1997;102;38-47.
10. Taskinen MR. Hyperlipidemia in diabetes. Bailliere Clin. Endocrinol Metab. 1990;4;743-75.
11. Howard BV. Lipoprotein metabolisim in diabetes mellitus. J. Lipid Res. 1987;28;613-28.
12. Zimmet PZ. Hyperinsulinaemia how innocent a bystander. Diabetes care. 1993;16:56-70.
13. Mc Laughlin T, Abbasi F, Cheal K, Cheal K, Chu J, Lamendola C, et al. Use of metabolic markers to identify overweight individuals who are insulin resistant. Ann Intern Med. 2003;139:802-9.
14. Gaziano JM, Hennekens CH, O'Donnell CJ. Fasting triglycerides, high density lipoprotein,and risk of myocardial infarction.Circulation. 1997;96:2520-5.
15. Levy FRI, Fridickson DS. Friedwald formula, In John D Bauer clinical laboratory methods. 9th ed. 1972:555.
16. Kahari SM, Virtanen KS, Tasiknen MR. HDLs containing apolipoprotiens A-I and A-II (LpA-I; A-II) as markers of coronary artery disease in men with NIDDM. Circulation. 1995;92:364-70.
17. Taskinen MR, Lipoprotein lipase in diabetes. Diabetes Metab Rev. 1987;3;551-70.
18. Taskinen MR, Lahdenpera S, Syvanne M. New insights into lipid metabolism in non-insulin-diabetes mellitus. Ann Med. 1996;28;335-40.
19. Edward, P, Feener, George, L. King. Vascular dysfunction in diabetes mellitus. Lancet. 199;350:09-13.
20. Velloso LA, Folli F, Sun XJ, White MF. Cross talk between the Insulin and angiotensin signaling systems. Proc. Nat. Acad. Sci. U.S.A. 1996;93:12490-5.
21. Miesenbock G, Patsch JR. Postparandial-hyperlipidemia. The search for the Atherogenic lipoprotein. Curr Opin Lipidol. 1992;3:196-201.
22. Grundy SM, Vega Gl. Two different views of the relationship of hypertriglyceridemia to coronary heart disease; implication for treatment. Arch Intern Med. 1992;152:28-34.