

Serum Lipid Profile in Non-insulin-dependent Diabetes Mellitus Associated with Obesity

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INTRODUCTION

Non-insulin-dependent diabetes mellitus (NIDDM) is an independent risk factor for coronary artery disease and risk of coronary disease is three to four fold increased in patients with NIDDM compared with non-diabetic population [1-4]. Patients with Type 2 diabetes are frequently affected by atherosclerotic vascular disease. These patients often have abnormalities of both quantity and quality of lipoproteins, that, among other factors, might be responsible for the increased incidence of vascular complications [5]. Several studies were conducted to find out the lipid abnormalities in diabetes mellitus and to ascertain the effect of anti-diabetic treatment on these abnormalities [4-9]. In this study we examined the serum lipid profile in obese Type 2 diabetics with fair to good control.

SUBJECTS and METHODS

This study was conducted on 50 obese NIDDM patients and 20 obese controls with normal glucose tolerance test (GTT) [10]. The criteria for selection of cases was :

1. A known diabetic on dietary control or on sulfonylurea drugs with the blood sugar in the acceptable range of control viz. fasting blood sugar 70-110 mg/dl; pre-prandial blood sugar 70-130 mg/dl; one hour post-prandial blood sugar 100-180 mg/dl and two hour post-prandial blood sugar 80-150 mg/dl [11].
2. Age of the patients/controls was 30-50 years.
3. Diabetic patients with overt complications of diabetes like nephropathy, neuropathy, retinopathy and obvious ischaemic heart disease (angina, myocardial infarction, 12 lead electrocardiogram abnormalities) were excluded.
4. Patients with any concurrent sickness like chronic liver disease, hypothyroidism were excluded.
5. Patients on drugs like diuretics, oral contraceptives (women) were excluded from the study.

The following anthropometric parameters were taken into consideration while characterizing the subjects as obese.

a) Weight and Height

Weight was recorded to the nearest kilogram (kg) with the subject standing on the weighing machine without shoes and using minimum of clothing. The same weighing machine was used for all the patients and the machine was tested with a known set of weights for any error [12]. Height was recorded with the subject erect, bare footed, feet together, back and heels against the upright bar of height scale, head upright in Frankfort horizontal plane 'look straight ahead'. The height measuring equipment consisted of a vertical bar with a steel tape attached. Attached perpendicularly to the vertical bar was a horizontal bar which was brought down snugly on the examinee's head [13].

Weight thus recorded (in kgs) was compared with the average weight/height tables for Indian males/females [14]. Those subjects whose weight was 20 % above the ideal weight were grouped as obese [15].

b) Body Mass Index (BMI)

Body Mass index was calculated from the formula; $BMI = \text{weight in kilograms} / (\text{height in meters})^2$ Patients were taken as obese if their body mass index was 27.8 and 27.3 for males and females respectively [16].

c) Triceps Skinfold Thickness (TSFT)

TSFT was measured to the nearest millimeter with a skinfold calliper halfway between the elbow and the acromion process of scapula over the triceps muscle with the skinfold parallel to the longitudinal axis of upper arm [13]. Subjects whose TSFT was more than 18.6 mm for males and 25.1 mm for females were taken as obese [17].

Subjects were labelled as obese if they fulfilled the above three criteria.

A detailed clinical history was taken and physical examination performed. Investigations performed included detailed haemogram including haemoglobin, total leucocytic count, differential leucocytic count, erythrocyte sedimentation rate and peripheral blood film, complete urine examination including 24-hour urinary proteins, blood urea, serum creatinine, serum sodium, potassium and detailed blood sugar profile

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including fasting, pre-prandial, one hour post-prandial and two hours post-prandial blood sugar, serum glutamic oxaloacetic transaminase, serum glutamic pyruvate transaminase, serum alkaline phosphatase, total proteins (serum albumin, globulin), X-ray chest and a 12 lead electrocardiogram was taken. Glucose tolerance test (GTT) with 75 gms glucose was performed on all control subjects and only those subjects who had normal GTT were included in the study [10].

For lipid estimations, blood samples were taken after overnight fast between 8 a.m. to 10 a.m. Different lipid fractions estimated included total lipids, serum cholesterol, high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), triglycerides and phospholipids [18-22].

Statistical analysis was done by Chi-square test.

RESULTS

The study was conducted on 50 obese NIDDM patients and 20 obese age and sex matched controls. The mean $\pm$ SD age of patients with NIDDM was 44.74 ± 4.27 (range 30-49 years) while the mean $\pm$ SD age of control was 40.6 ± 4.8 (range 30-48 years). Out of 50 patients 29 (58%) were males and 21 (42%) were females. Among control subjects 12 (60%) were males and 8 (40%) were females (Table 1).

Table 1
Age and sex distribution of study population

	Obese NIDDM (50)	Obese control (20)
Age in years (range)	30-49 years	30-48 years
Mean $\pm$ SD	44.76 ± 4.23	40.6 ± 4.8
Sex distribution		
Males	29 (58%)	12 (60%)
Females	21 (42%)	8 (40%)

Table 2 gives the detailed anthropometric parameters viz., weight in kgs, height in cms, body mass index and triceps skin fold thickness of patients and control subjects.

Obese diabetics when compared to obese control subjects showed statistically significant increase in the levels of serum total lipids ($P < .001$), serum total cholesterol ($P < .001$), serum triglycerides ($P < .001$), serum LDL - cholesterol ($P < .001$) while serum HDL-cholesterol levels did not show statistically significant difference in the two group ($P > .05$) (Table 3).

Table 2
Anthropometric parameters of the subjects

	Obese NIDDM	Obese control
Weight in kgs		
Range	64-92	65-100
Mean $\pm$ SD	77.83 ± 6.88	78.05 ± 6.90
Height in cms		
Range	150-180	153-180
Mean $\pm$ SD	165.96 ± 7.4	164.25 ± 6.9
BMI		
Range	27.4 - 30.01	27.99 - 31.24
Mean $\pm$ SD	28.25 ± 0.61	28.86 ± 1.05
Triceps skinfold thickness (in mm)		
Range	20.5 - 31.5	21.5 - 31.5
Mean $\pm$ SD	25.38 ± 3.19	26.1 ± 2.83

Table 3
Lipid Profile

	Obese NIDDM	Obese control	p value
Total lipids			
Range	720-892	501-736	
Mean $\pm$ SD	797.68 ± 40.79	647.35 ± 65.68	<.001 HS
Total Cholesterol			
Range	235-300	150-260	
Mean $\pm$ SD	263.02 ± 18.01	215.9 ± 33.30	<.001 HS
Triglycerides			
Range	200-352	86-230	
Mean $\pm$ SD	257 ± 24.70	189.25 ± 40.35	<.001 HS
HDL-cholesterol			
Range	30-65	35-60	
Mean $\pm$ SD	46.48 ± 9.2	47.25 ± 6.63	>.05 NS
LDL-cholesterol			
Range	115-192	70.8-198	
Mean $\pm$ SD	164.96 ± 16.8	135.32 ± 35.99	<.001 HS
Phospholipids			
Range	200-320	139-286	
Mean $\pm$ SD	252.82 ± 23.54	213.15 ± 39.97	<.001 HS

HS = Highly significant

NS = Not significant

DISCUSSION

Accelerated Coronary and peripheral vascular atherosclerosis is one of the most common and serious chronic complications of long term diabetes mellitus. Along with other risk factors such as hypertension, smoking, obesity etc., increasing importance has been given to secondary hyperlipidaemias in the causation of accelerated atherosclerosis [23]. Hyperlipidaemia as a metabolic abnormality is frequently associated with diabetes mellitus. Its prevalence is variable, depending on the type and severity of diabetes, glycaemic control, nutritional status, age and other factors.

The most characteristic lipid abnormality in diabetics is hypertriglyceridaemia, with or without associated increase in plasma cholesterol [8-9]. In our study, obese diabetics when compared to obese control subjects showed statistically significant increase in the levels of serum total lipids ($P < .001$), serum total cholesterol ($P < .001$), serum triglycerides ($P < .001$), serum LDL-cholesterol ($P < .001$) and serum phospholipids ($P < .001$). Serum HDL-cholesterol levels did not differ significantly ($P < .05$) in the two groups. Cohen et al (1979) showed significant increase in the level of serum cholesterol and LDL cholesterol in obese diabetics when compared with obese controls. In their study, serum HDL-cholesterol levels did not differ significantly in the two groups [24]. Sharma (1970) and Jain (1980) observed increase in the levels of serum total lipids, total cholesterol, serum triglycerides and serum phospholipids in diabetic subjects as compared to normal controls [25, 26]. The studies of Santen et al (1972) and Peret et al (1974) observed mean serum triglyceride levels higher in obese diabetics in comparison to obese control subject [27,28]. Bijlani et al (1984) found HDL-cholesterol to be significantly lower in obese diabetics as compared to normal weight diabetics [29].

In preliminary studies, no defect in LDL receptor binding was found in the skin fibroblast from diabetics [30]. However, when the interaction of fibroblast from normal individuals with the LDL isolated from diabetics was studied, a significant impairment was observed in diabetic LDL internalization and degradation [31]. It has been suggested that chemical modification of the LDL particle itself (like non-enzymatic glycosylation of LDL) [31] might result in its increased incorporation in the arterial wall via a receptor independent pathway [32]. The critical range of glycaemia sufficient to induce LDL glycosylation in vivo remains to be determined and would obviously be of great interest. Most of the diabetic patients are found to have variable combination of triglyceride overproduction or under utilization. In severe insulin deficiency, lipoprotein lipase (LPL) activity is markedly impaired [33,34]. However, in mild to moderately severe non-insulin requiring diabetics LPL activity is relatively intact [34]. In such diabetics, endogenous triglyceride synthesis is enhanced [35], particularly in the presence of obesity and adequate amounts of insulin.

Many studies have strongly suggested an inverse correlation of HDL-cholesterol level with the development of ischaemic heart disease [36-38]. Most of the studies have revealed the inverse relationship of HDL-cholesterol with atherosclerosis to be independent of other lipid abnormalities. In a study of

165 diabetic out patients at the Joslin clinic, HDL-cholesterol was lower in non-insulin-dependent diabetics and normal in insulin-dependent diabetics of both sexes, while total cholesterol was similar in the two groups [39]. These observations can be at least partly explained by the known inverse correlation of HDL-cholesterol with adiposity and triglyceride levels [40-42]. In some studies, HDL-cholesterol or LDL/HDL-cholesterol ratios have been shown to be inversely correlated with prevailing blood glucose levels [43, 44] or with glycosylated haemoglobin levels, as an index of blood glucose control [44, 45]. However, this has not been confirmed by other [46,47].

This study has clearly shown that all lipid fractions (except HDL) are abnormally elevated in obese diabetics when compared with obese controls. There are studies which seem to suggest that the lipoprotein distribution in Type 2 diabetes mellitus is not significantly altered by the degree of metabolic control [48-50].

Realizing that most of the diabetics have a high probability of developing cardiovascular and cerebrovascular disease [51], is essential that in an individual who is obese and diabetic (two strong risk factors for coronary artery disease) their lipid abnormalities be properly taken care of, if morbidity and mortality in a diabetic is to be significantly altered. Several studies have shown a salutary effect of physical activity on HDL-cholesterol [52,53] although the degree and frequency of activity needed, remains to be established. Smoking has been shown to adversely effect HDL-cholesterol [54]. Some studies with high fibre diets have suggested significant improvement in plasma triglyceride levels and in HDL/LDL cholesterol ratio [55, 56]. Dietary rape seed oil, margarine rich in sitostanol ester was effective for lowering VLDL and LDL cholesterol and increasing HDL-cholesterol in hypercholesterolaemic non-insulin-dependent diabetic subjects [57].

REFERENCES

1. Garcia MJ, McNamara PM, Gordon T, Kannel WB. Morbidity and mortality in diabetics in the Framingham population, sixteen year follow-up study. *Diabetes* 1974; 23 : 105.
2. Kannel WB, McGee DL. Diabetes and cardiovascular risk factors: the Framingham study. *Circulation* 1979; 59: 8.
3. Stamler J, Wentworth D, Neaton J, Schoenberger JA, Feigal D for the MRFIT Research Group.. Diabetes and risk of coronary, cardiovascular and all causes, mortality findings for 356,000 men screened by the

- Multiple Risk Factor Intervention Trial (MRFIT). *Circulation* 1984 ; 70: (Suppl 2) :11.
4. Puir J, Twillet J, Huby T, et al. Association of elevated lipoprotein (A) levels and coronary heart disease in NIDDM patients, relationship with apolipoprotein (A) phenotypes. *Diabetologia* 1994; 37: 585.
 5. Assmann G, Schute H. The prospective cardiovascular Minster (Procam) study; prevalence of hyperlipidaemia in persons with hypertension and/or diabetes mellitus and the relationship to coronary heart disease. *Am Heart J* 1988; 116: 1713.
 6. Ostrander LD, Francis T, Hayer NS, et al. The relationship of cardiovascular disease to hyperglycaemia. *Ann Intern Med* 1965; 62: 188.
 7. Ducimetiere P, Eschwege E, Papoz L, et al. Relationship of plasma insulin levels to the incidence of myocardial infarction and coronary heart disease mortality in middle age population. *Diabetologia* 1980; 19: 205.
 8. Goldberg RB. Lipid disorders in diabetes. *Diabetes Care* 1981; 4 : 561.
 9. Taskinen MR. Hyperlipidemia in diabetes. *Clin Endocrinol Metab* 1990; 4 : 743.
 10. WHO study group report on diabetes mellitus. WHO technical report series 727, WHO Geneva 1985.
 11. Skyler SJ, Michael LR. Intensive treatment of Type 1 diabetes mellitus. In : *Diabetes Mellitus, management and complication* . Jerrold M. Olefsky, Robert SS (eds). 1985; 1 : 32.
 12. Verma BL, Kumar A, Srivastava RN. Measurement of body build based on weight/height, an index for adults in an Indian population. *Ind J Pub Health* 1982; 26.
 13. Frisancho AR. New standards of weight and body composition by frame size and height for assessment of nutritional status in adults and elderly. *Amm J Clin Nutr* 1984; 40 : 808.
 14. Antia FP. *Clinical Nutrition* 2nd Ed. R Dayal, Delhi 1973; 642.
 15. Olefsky JM. Obesity In: *Harrison's Principles of Internal Medicine*. 12th Ed. McGraw Hill book Company , New York, 1991; 411.
 16. Olefsky JM. Diabetes mellitus, In *cecil textbook of Medicine* 18th Ed. Wynaagarden and Smith Jr. Eds; WB Saunders Int ED. 1992; 1291.
 17. Bray GA. Obesity In: *Disease a Month*. Book Med Publisher Inc. Chicago London, 1979; 26.
 18. Frings CS, Dunn RT. A colorimetric method of determination of total serum lipids based on sulphophosphovanillin reaction. *Am J Clin Pathology* 1970; 53 : 89.
 19. Allain CC. Enzymatic colorimetric method for estimation of serum cholesterol . *Clin Chemistry* 1974; 20: 470.
 20. Lopes-Virefla MF. Enzymatic colorimetric method for estimation of HDL-cholesterol. *Clin Chem* 1977; 23: 288.
 21. Varley H, Gowenlock AH, Bell M. *Lipids and Lipoproteins In: Proteins clinical biochemistry* 5th ed, William Heinemall Medical books Ltd London, 1980; 1.
 22. Bucolo D, David H. Quantitative determination of serum triglycerides by use of enzymes. *Clin Chem* 1973; 19 : 476.
 23. Dunn FL. Treatment of lipid disorders in diabetes mellitus. *Med Clin North America* 1988; 72.
 24. Cohen AM, Fidel J. Diabetes, blood lipids, lipoproteins, change of environment. *Met* 1979; 28 : 7.
 25. Sharma D, Bansal BC, Prakash C. Serum lipid studies in thin insulin dependent diabetics below the age of 30 years. *J Ind Med Ass* 1970; 9 : 54.
 26. Jain AP, Gupta DP. Study of blood, lipids diabetes without any manifest vascular complications JDAI 1980; 20.
 27. Santen JR, Park W Willis, Stefan S. Atherosclerosis in diabetes mellitus correlation with serum lipid levels, adiposity and serum insulin levels. *Arch Int Med* 1972; 130.
 28. Paret AD, Rowes A, Shahmanesh M. Blood lipids in treated diabetics. *Diabetologia* 1974; 10: 115.
 29. Bijlani PK, Shah Kokila, Raheja BS. HDL cholesterol in diabetics. *JAPI* 1984; 32.
 30. Chait A, Biermann EL, Albers JJ. Low density lipoprotein receptor activity in skin fibroblasts cultured from diabetic donors. *Diabetes* 1979; 28 : 914. 0
 31. Lopes-Virefla MF, Sherer GK, Lees AM, et al. Surface binding, internalization and degradation by cultured human fibroblasts of low density lipoproteins isolated from Type 1 (insulin-dependent) diabetic patients. Changes with metabolic control. *Diabetologia* 1982 ; 22 : 430.
 32. Gonen B, Baenzider J, Schonfeld G, et al. Non-enzymatic glycosylation of low density lipoproteins in vitro. Effects on cell interactive properties. *Diabetes* 1981; 30 : 875.
 33. Brunzell JD, Chait A, Beirman EL. Pathophysiology of lipoprotein transport. *Metabolism* 1978; 27 : 1109.

34. Nikkila EA, Huttunen JK, Enholm C. Post-heparin plasma lipoprotein lipase and hepatic lipase in diabetes mellitus-relationship to plasma triglyceride metabolism. *Diabetes* 1977; 26: 11.
35. Abrams JJ, Ginsberg H, Grundy SM. Metabolism of cholesterol and plasma triglycerides in non-ketotic diabetes mellitus. *Diabetes* 1982; 31 : 903.
36. Castelli WP, Doyle JT, Gordon T, et al. HDL-cholesterol and other lipids in coronary heart disease : The cooperative lipoprotein phenotyping study. *Circulation* 1977; 55 : 767.
37. Miller NE, Forde OH, Thelle DS, Mjos OD. The Tromso heart study. High density lipoprotein and coronary heart disease : a prospective case controlled study. *Lancet* 1977; 1: 965.
38. Goldbourt, U, Medalie JH. High density lipoprotein cholesterol and incidence of coronary heart disease; the Israel Ischaemic Heart Disease study. *Am J Epidemiol* 1979; 109 : 296.
39. Ganda OP, Hayes EJ, Soledner Js, et al. Alterations in high density lipoprotein-cholesterol (HDL-cholesterol) and its relationship to control of diabetes. 10th Congress of the International Diabetes Federation, Vienna, Austria 1979;72 : 9.
40. Gordon T, Castelli WP, Hjortland MC et al. High density lipoproteins as a protective factor against coronary heart disease: the Framingham study. *Am J Med* 1977; 62: 707.
41. Kannel WB, Castelli WP, Gordon T. Cholesterol in the prediction of atherosclerotic disease. New perspectives based on Framingham study. *Ann Intern Med* 1979; 90 : 85.
42. Schaeffer E, Levy RI, Anderson DW, et al. Plasma triglycerides in regulation of HDL-cholesterol levels. *Lancet* 1978; 2: 391.
43. Lopes-Verefla MF, Stone PG, Colwell JA. Serum high density lipoproteins in diabetic patients. *Diabetologia* 1977; 13: 285.
44. Lopes- Verefla MF, Wohltmann HJ, Loadhoet CB, Buse MG. Plasma lipids and lipoproteins in young insulin-dependent diabetic patients. *Diabetologia* 1981; 21: 216.
45. Schmitt JK, Poole JR, Lewis SB, et al. Haemoglobin A, correlated with the ratio of low to high-density lipoprotein cholesterol in normal weight Type-2 diabetics. *Metabolism* 1982; 31: 1084.
46. Boucher BJ, Yudhin J. Diabetic control and HDL-cholesterol level. *Lancet* 1978; 2: 269.
47. Elkeles RS, Wu J, Hambley J. Haemoglobin A, blood glucose and high-density lipoprotein-cholesterol in insulin-requiring diabetics. *Lancet* 1978; 2 : 547.
48. Laakso M, Voutilainen F, Sarlund H, et al. Serum lipids and lipoproteins in middle-aged non-insulin-dependent diabetics. *Atherosclerosis* 1985; 56: 271.
49. Billingham MS, Miles JJ, Bailey CJ, Hall RA. Lipoprotein subfraction composition in non-insulin-dependent diabetes treated with diet, sulphonylurea and insulin . *Metabolism* 1989; 38: 850.
50. Kennedy AL, Lappin TRJ, Lavery TD, et al. Relation of high density lipoprotein cholesterol concentration to type of diabetes and its control. *Br Med J* 1978; 2: 1191.
51. Colwell JA, Vascular thrombosis in Type 2 diabetes mellitus. *Diabetes* 1993 ; 42: 8-11.
52. Wood PD, Haskell W, Klein H, et al. The distribution of plasma lipoproteins in middle-aged male runners. *Metabolism* 1976; 25: 1249.
53. Miller NE, Rao S, Lewis B, et al. High density lipoproteins and physical activity. *Lancet* 1979; 1: 111.
54. Hulley S, Ashman P, Kuller L, et al . HDL- cholesterol levels in the Multiple Risk Factor Intervention Trial by the MRFIT Research Group. *Lipids* 1979; 14: 119.
55. Jenkins DJA. Dietary fibre, diabetes and hyperlipidaemia. *Lancet* 1979; 2 : 1287.
56. Simpson HCR, Simpson RW, Lousley S, et al. A high carbohydrate leguminous fibre diet improves all aspects of diabetic control. *Lancet* 1978;1 : 1055.
57. Gylling H, Miettinen TA. Serum cholesterol and lipoprotein metabolism in hypercholesterolemic NIDDM patients before and during sitostanol ester-margarine treatment. *Diabetologia* 1994; 37 : 773.