

A STUDY OF DYSLIPIDEMIA AND PLATELET ADHESIVENESS IN NON-INSULIN DEPENDENT DIABETES MELLITUS

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Abstract : The present study included 50 controls (age 34-64 years) and 50 NIDDM subjects (age 32-72 years) from the diabetic clinic of Government Medical College, Nagpur. It was undertaken with the aim of investigating obesity indices (i.e. body mass index, skin fold thickness, waist hip ratio and % fat in the body); lipid profile (including serum total cholesterol, triglyceride, VLDL, LDL and HDL-cholesterol) levels and platelet adhesiveness in both the groups. On comparison, plasma glucose levels were higher in NIDDM ($P > 0.05$); obesity indices, cholesterol, triglyceride, VLDL, LDL and platelet adhesiveness index were higher, and HDL levels low in NIDDM group as compared to controls ($P < 0.01$).

Obesity, dyslipidemia and increased platelet adhesiveness are interconnected and make diabetics more susceptible to arterial disease with increased risk of vascular episodes.

Key words : NIDDM
platelet adhesiveness
dyslipidemia
obesity indices

INTRODUCTION

Diabetes affects at least 30 million people throughout the world. Overall prevalence among Indians was 1.73% (1). Non-insulin dependent diabetes mellitus (NIDDM), the commonest variety of diabetes, is characterized by either deficiency of insulin or resistance to action of insulin or both. Insulin resistance is also seen in obesity which often accompanies NIDDM. Insulin has important effects on key steps in the metabolism of lipids and lipoproteins which are altered in diabetes,

possibly leading to dyslipidemia. The greater susceptibility of persons having diabetes to vascular complications and atherosclerotic disease led to the idea that changes in platelet adhesiveness might occur in diabetes. This cross sectional study assesses and compares levels of plasma glucose fasting and postmeal, total serum cholesterol, triglyceride, HDL, LDL and VLDL in control and NIDDM subjects. Platelet adhesivity index in control population has also been compared with NIDDM subjects.

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METHODS

A total of 50 confirmed cases of NIDDM (35 males and 15 females) of 32–67 years age and 50 controls (32 males and 18 females) of 34–64 years age were included in the study. The selection criteria for NIDDM subjects was post meal blood sugar <200 mg% (controlled diabetes) (2).

They had not received oral antidiabetics, cholesterol lowering agent and hormones for one month. Controls had not suffered from diabetes, atherosclerosis, thrombotic disease or IHD. No subjects had a family history of diabetes. None had smoked or had diseases such as nephropathy, neuropathy or any other complication of diabetes. All were on mixed diet and avoided high fat and sugar. All were instructed to take their dinner before 10 p.m. and report for investigations next morning at 9 a.m.

The following investigations were performed.

1. Measurement of body mass index, skinfold thickness and waist/hip ratio.
2. Estimation of a) Blood glucose fasting and postmeal, b) Serum cholesterol, c) Serum triglyceride, d) Serum HDL cholesterol and e) Platelet adhesivity, VLDL and LDL were estimated by computation.

Body mass index was measured by the formula :

$$\text{BMI} = \text{weight in kg}/(\text{Height in meters})^2$$

Percent fat in body was calculated from BMI using the following formula :

$$\text{In males, \% fat} = 1.218 (\text{Wt}/\text{Ht}^2) - 10.13$$

$$\text{In females, \% fat} = 1.48 (\text{Wt}/\text{Ht}^2) - 7 (3)$$

Skin fold thickness was measured using UNA skin fold caliper at four sites i.e. triceps, biceps, subscapulars and suprailiac.

Waist/hip ratio was measured with simple tape at the levels of waist and hip of the subjects.

Fasting blood sample of about 8 ml from antecubital vein was collected by a glass syringe thinly smeared with liquid paraffin. 1.8 ml of blood was transferred to a glass vial coated with paraffin wax containing 0.2 ml of 3.8% sodium citrate and mixed well. This blood was used for platelet adhesivity. Two ml blood was transferred to fluoride bulb containing sodium fluoride 10 mg/ml for blood glucose estimation. Remaining blood was transferred to plain bulb for estimation of serum cholesterol, triglyceride and HDL cholesterol.

Postmeal blood sample was collected 1½ hour after the meal. Blood glucose estimation was done by GOD-POD i.e. glucose oxidase peroxidase method (4). Serum cholesterol and Triglyceride was measured using CHOD-PAP method (Boehringer Mannheim Ltd) (5). HDL cholesterol was measured using well established precipitating properties of phosphotungstic acid to precipitate non HDL cholesterol (6). VLDL cholesterol was measured by Friedwald's formula (7). LDL cholesterol is measured by the formula :

LDL cholesterol = Total cholesterol - (HDL+VLDL)

RESULTS

To measure platelet adhesivity index platelet count was done by method of Kristensons modified by Lampert (8) and the remaining sample was treated by Wright's method (9) and platelet adhesivity index calculated by following formula :

$$\text{Platelet adhesivity index} = (\text{Initial count} - \text{Final count}) \times 100 / \text{intial count}$$

Significance of the results was analysed by Student's test.

Body mass index, percent fat in body, skinfold thickness and waist hip ratio values are more in females as compared to males in both control as well as NIDDM groups. The values were higher in NIDDM subjects as compared to controls (P<0.05) Table I.

The values of obesity indices were higher in NIDDM group than in controls (P<0.01) Plasma glucose levels were also higher in NIDDM subjects than in controls but only marginally significant (P>0.05), Table II.

TABLE I: Characteristics of the study group.

Characteristics	Control subjects		P value	NIDDM patients		P value
	Males (n=32)	Females (n=18)		Males (n=35)	Females (n=15)	
Age in yrs	34-64	34-64		32-72	32-72	
BMI (kg/M ²)	21.6±2.8	21.8±3.7	<0.05	24.2±3.4	24.4±3.67	<0.05
% Fat	16.17	19.35	<0.05	25.26	29.112	<0.05
SFT (mm)	41.6±3.5	42.5±7.6	<0.05	43.8±4.5	45.4±6.37	<0.05
WH Ratio	0.74±0.05	0.75±0.11	<0.05	0.78±0.03	0.81±0.04	<0.05
Fasting Plasma Glucose	86.68±11.10	86.72±16.1	<0.05	95.6±17.67	103±21.0	<0.05
Post Meal Plasma Glucose	128.12±14.0	126.53±20.7	<0.05	140.4±29.90	141±35.9	<0.05

TABLE II: Obesity indices and plasma glucose in the study group.

Characteristics	Control (n = 50)	NIDDM (n = 50)	P value
Mean BMI (kg/M ²)	22.13±2.5	24.34±3.5	<0.01
Mean SFT (mm)	43.18±4.98	45.5±5.7	<0.01
Mean Waist/hip ratio	0.76±0.05	6.79±0.4	<0.01
% Fat	16.17±3.7	19.35±4.7	<0.01
Fasting Plasma Glucose (mg/dl)	88.38±1.8	98.06±18.87	>0.05
Post Meal Plasma Glucose (mg/dl)	128.7±13.6	140.8±21.4	>0.05

TABLE III: Lipid profile and platelet adhesiveness in the study group.

Parameters	Control (n = 50)	NIDDM subjects (n = 50)	P value
Mean serum cholesterol (mg/dl)	158.8±22.3	222.7±60.5	<0.01
Mean serum triglyceride (mg/dl)	132.8±43.4	178.9±89.5	<0.01
Mean serum VLDL (mg/dl)	26.5±3.52	35.78±17.8	<0.01
Mean serum LDL (mg/dl)	57.24±26.7	142.92±36.9	<0.01
Mean serum HDL (mg/dl)	75±10.1	44±5.8	<0.01
Mean platelet adhesivity (%)	27.61±2.5	36.93±3.6	<0.01

Mean serum levels of cholesterol, triglyceride, VLDL, LDL were higher and HDL levels lower in NIDDM than in controls ($P < 0.01$) Table III.

Mean platelet adhesivity index in percentage was higher in NIDDM subjects than in controls ($P < 0.01$). No correlation was found between duration of diabetes and mean serum levels of the parameters of lipid profile and platelet adhesivity index when ANOVA test was applied.

DISCUSSION

Obesity, central distribution of fat, low level of physical activity and high fat diet have close association with NIDDM (10). Now it is known that the adipocyte specific hormone leptin, the product of the obese (ob) gene, regulates adipose tissue mass through hypothalamic effect on satiety and energy expenditure (11). Obesity is associated with increased plasma FFA levels that cause peripheral and hepatic insulin resistance. Insulin resistance and FFA induced gluconeogenesis stimulate insulin secretion. The result is no or minimal change in hepatic glucose production (HGP). But in obese subjects who are genetically

predisposed to develop NIDDM, FFA fails to stimulate insulin secretion. This, together with peripheral glucose underutilization (attributable to uncompensated peripheral insulin resistance), leads to increased HGP that results in NIDDM (12, 13).

Besides this the biological process of aging leads to loss in the ability to maintain glucose homeostasis. Age-related deterioration in glucose tolerance may be due to failing insulin secretory capacity or impaired insulin action, or both (14).

In NIDDM subjects increased levels of serum cholesterol as compared to control (Table III) can be due to various reasons. (a) Over stimulation of HMG-CoA reductase enzyme by glucagon which is rate limiting for cholesterol synthesis. (b) Defective catabolism of cholesterol into bile acids also leads to more cholesterol in blood. (c) More VLDL in plasma causes hypercholesteremia because VLDL carries about 20% of its total lipid content as cholesterol (15). (d) Cholesterol absorption in NIDDM subjects was significantly lower while cholesterol synthesis significantly higher (16).

Statistically very significantly raised levels of serum triglyceride and serum

VLDL cholesterol were found in NIDDM as compared to control (Table III). NEFA (non esterified fatty acids) causes hepatic triglyceride synthesis. The release of it as VLDL is facilitated by insulin resistance (17). This increased production of VLDL is associated with clearance defect, including lower fractional catabolic rate for VLDL-TG. Lower adipose lipoprotein lipase (LPL) activity is dependent upon insulin and is rate limiting for triglyceride degradation (18).

Serum LDL cholesterol is higher because VLDL is precursor of LDL and raised VLDL may lead to increased LDL levels associated with decreased LDL catabolism. LDL receptor is upregulated by insulin but in NIDDM due to insulin resistance, there is less uptake of LDL (19).

The decrease in HDL level is statistically highly significant in NIDDM subjects when compared to controls ($P < 0.01$). This decrease may be due to enhanced activity of LCAT (Lysolecithin acyl transferase) which also causes hypertriglyceride mia. In LDL rich cholesterol and phospholipid the enhanced LCAT activity promotes the transfer of activated fatty acids to cholesterol resulting in formation of lysolecithin which in turn

causes triglyceride formation. This enhanced activity impairs the formation of HDL from LDL and hence HDL-cholesterol is reduced significantly in NIDDM (20).

The findings in present study are similar to various other studies conducted in different parts of the world (18, 21, 22, 23).

Patients of diabetes mellitus have an increased tendency to intravascular thrombosis and have hypercoagulability of blood. So our finding of increased platelet adhesiveness is significant. The platelet rich plasma of diabetic patients synthesizes greater quantities of prostaglandin E like materials after exposure to various concentratins of ADP, epinephrine and collagen and the platelets are more sensitive to aggregating effects of prostaglandin precursor arachidonic acid. Subsequent metabolic products of prostaglandin, thromboxane A2 is believed to be responsible for platelet release reaction as well as aggregation (24). The raised thromboglobulin is result of early and diffuse changes in diabetic vascular endothelium which might affect platelet function before the lesion becomes clinically detectable (25).

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