

## Role of Lipids in type 2 diabetes mellitus for causation of coronary artery disease

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### Abstract

Diabetes is characterized by chronic hyperglycemia and disturbances of carbohydrate, protein and lipid metabolism. The present study was undertaken to research the association between serum lipid profile, its abnormalities and the increase risk of coronary artery disease. The study comprised of total 60 subjects out of which 30 were diabetic patients with T2D and 30 healthy individuals, both from the age group 35-50 years. The results indicated that there was a considerable increase in the lipid and its parameters.

**Keywords:** Diabetes mellitus, HDL-c, LDL-c, Lipid profile, Total cholesterol, VLDL-c.

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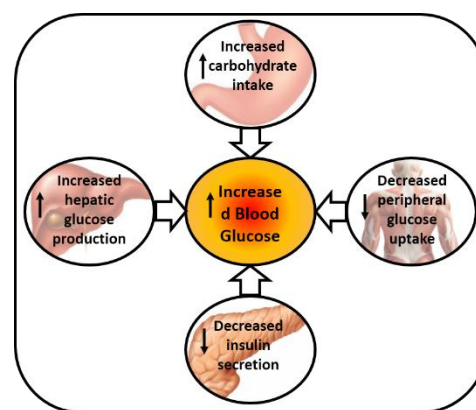
### Introduction

Diabetes mellitus (DM) is a chronic disease, which occurs when the pancreas does not produce enough insulin, or when the body cannot effectively use the insulin it produces. Type 2 diabetes (T2D) (formerly called non-insulin-dependent or adult-onset diabetes) is caused by the body's ineffective use of insulin. Instead of moving into your cells where it's needed for energy, sugar builds up in the bloodstream. Exactly why this happens is uncertain, although it's believed that genetic and environmental factors play a role in the development of type 2 diabetes. Being overweight is strongly linked to the development of T2D, but not everyone with T2 is overweight.<sup>1</sup>

Tissue resistance to insulin-mediated glucose uptake is now recognized as a major pathophysiologic determinant of T2D.(Fig. 1) There has been an explosion of research that has been established insulin resistance both as a clinical precursor of diabetes and a possible explanation for the associated injurious alterations in cardiovascular health. Insulin resistance compels the pancreatic islet cells to hyper secrete insulin and at some stage the pancreas is unable to secrete enough insulin to overcome the insulin resistance and this leads to – cells exhaustion and ultimately to glucose intolerance and DM. The clinical consequences of reduced insulin sensitivity are not limited to diabetes, but also encompass other chronic conditions like dyslipidaemia and hypertension. The net action of insulin is to decrease the blood

glucose level by inhibiting gluconeogenesis and stimulating glycolysis. Insulin also has lipogenic

action promoting lipogenesis and inhibiting lipolysis.<sup>2</sup> Protein synthesis is stimulated and protein degradation is retarded by insulin.<sup>3</sup>



**Fig. 1. Pathophysiology of T2D**

Hyperlipidemia has been defined in the past as plasma cholesterol and triglyceride levels that exceed 'normal' levels. Hyperlipidemia is a metabolic disorder, which is secondary to diabetes. The increased risk of coronary artery disease in subjects with DM can be partially explained by the lipoprotein abnormalities associated with DM. The most common lipid abnormalities is hypertriglyceridemia and low levels of high –density lipoprotein. Its prevalence is variable depending upon the type and severity of diabetes, glycemic control, nutritional status, age, life style and other factors.<sup>4</sup>

Dyslipidemias was traditionally classified by patterns of elevation in lipids and lipoproteins. A

more practical system categorizes dyslipidemias as primary and secondary. The population suffering from diabetes tend to have an atherogenic combination of high triacylglycerides (TG), high low density lipoprotein (LDL) and low high density lipoprotein (HDL).<sup>5</sup>

The relationship between the elevation of serum lipids and vascular complications of diabetes has long been of interest because both tend to occur with greater frequency in diabetics than in general population. In the light of this knowledge it is now possible to make a more accurate appraisal of the relationship between diabetes, its vascular complications and serum lipids. It is hence essential to know the extent of hyperlipidemia in the diabetic patients. In addition to the clinical examination the laboratory investigation will definitely aid the physician in the diagnosis and prognosis, who can then suggest the appropriate diet therapy and exercise.

### Materials and Methods

The following study was carried out in TNMC & BYL Nair Ch. Hospital, Mumbai. Total enrolled subjects were 60 out of which 30 were diabetic patients with T2D and 30 healthy individuals, both from the age group 35-50 years.

**Inclusion and exclusion criteria:** Subjects with T2D without any systemic disease were included. Subjects with systemic disease like HIV, cancer etc. were excluded from the study. Subjects who consumed tobacco in any forms (smoking, chewing) were also excluded from the study. The study was approved by the Institutional ethics committee. Written informed consents were obtained from the subjects.

**Sample collection:** The subjects were given prior information regarding collection. The patients were instructed about 12 -13 hours of fasting

before collection. 7ml of fasting blood sample was collected in a heparinized tube and the plasma was allowed to separate. The samples were stored at 4°C if required. The collected samples were later used for biochemical estimations of TG's, cholesterol, HDL-cholesterol.

Serum cholesterol was evaluated by Zak's method.<sup>6</sup> Serum TG by Hexane extraction method,<sup>7</sup> HDL-cholesterol by Watson Precipitation method<sup>6,8</sup> and very low-density lipoprotein (VLDL) and LDL cholesterol by Friedwald's formula.<sup>9</sup>

### Statistical analysis

Statistical analysis was done using students 't' test. The values obtained were tabulated and mean and standard deviation (SD) of all the parameters were calculated. The test of significance applied was ANOVA (Analysis of Variance) for comparison. p value ≤ 0.001 was considered as statistically significant.

### Results and Discussion

The current study was undertaken to understand if the patients with T2D resulted in changes in lipid metabolism and thereby increased risk of coronary artery disease (CAD). The results indicated that there is a considerable increase in the lipid and lipoprotein concentration of T2D patients as compared to healthy controls leading to increase in coronary risk factors.

The concentrations of blood Total cholesterol, TG's, HDL-c, LDL-c and VLDL-c cholesterol levels respectively in the sera of 30 diabetic patients (T2D) and of 30 normal healthy individuals (Table 1)

**Table 1: Concentrations of all parameters in the sera of 30 diabetic and 30 healthy individuals (mg/dl)**

	Total Cholesterol		TG's		HDL-c		LDL-c		VLDL-c	
	Control	Test	Control	Test	Control	Test	Control	Test	Control	Test
Range (mg/ml)	170.3-237.0	263.7-418.5	81-55-119.4	174.7-378.6	29.62-59.25	13.3-35.5	94.81-159.7	155.5-334.2	16.31-23.88	40.77-93.2
Mean (mg/dl)	182.7	300.2	94.65	283.6	45.67	22.91	114.03	226.6	18.92	57.03
S.D	±29.89	±65.69	±13.04	±62.78	±14.24	±17.68	±36.99	±60.12	±18.92	±15.16
S.E	5.75	12.64	2.72	13.10	2.74	1.47	7.76	12.29	0.53	3.10
t	-	6.08	-	7.37	-	6.71	-	5.57	-	4.31
p	-	<0.0005	-	<0.0005	-	<0.0005	-	<0.0005	-	<0.0005

Plasma TG in the diabetic patients averaged 283.65 mg/dl showing considerable variation from patient to patient. Total cholesterol and HDL

cholesterol in diabetic patients averaged 300.29 mg/dl and 22.91 mg/dl respectively.

The HDL-c reduces the body's cholesterol by boosting the removal of cholesterol from

peripheral tissues. Therefore, T2D is usually seen associated with low HDL -c levels.<sup>10</sup>

Higher levels of total cholesterol and TG's along with lower HDL-c in diabetic patient may be a very sensitive indication of cardiovascular risk.

LDL-c in the normal healthy subjects averaged 114.03, but a significant increase was observed ( $p < 0.0005$ ) compared to the healthy control.

Diabetics showed higher VLDL-c concentrations (57.03 mg/dl) showing high significance ( $p < 0.0005$ ).

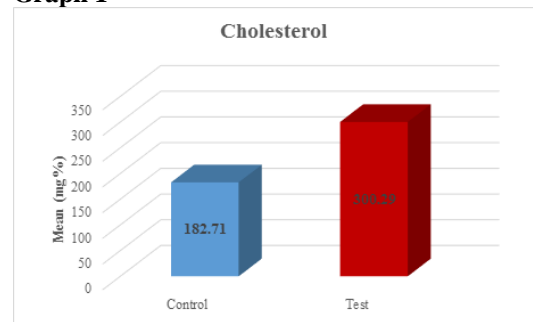
Highly positive correlation is seen between total cholesterol and HDL-c, showing high significance (0.58) indicating that both the parameters are directly proportional. A partial negative correlation is observed in between total cholesterol and HDL-c, showing high significance (0.66) indicating that both the parameters are inversely proportional. A moderate negative correlation is seen between TG and HDL-c showing moderate significance (0.47).

Hyperglycemia successively rapids the formation of cholesterol esters from HDL to small particles VLDL, further decreasing the HDL-c levels. In addition, HDL also acts as a substrate for enzyme lipase which converts it into smaller fractions that easily cleared from the plasma. This results in low HDL cholesterol level and higher TG levels, which may improve with improved glycaemic control.<sup>11-13</sup>

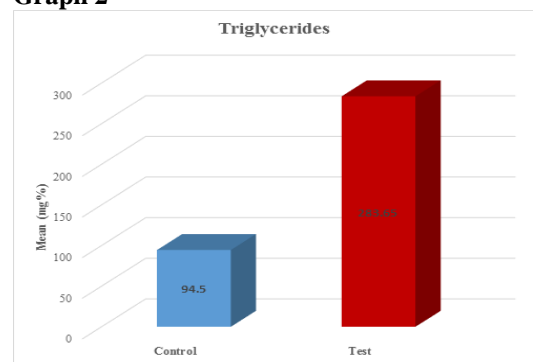
The most characteristic lipid abnormality in diabetes is hypertriglyceridemia. The present study shows sharp increase in the concentrations of total cholesterol, triglycerides, LDL and VLDL cholesterol, whereas levels of HDL cholesterol were found to have decreased. Taken together, these observations suggest that diabetes has an adverse effect on lipid profile of the subject, thus increasing the risk of coronary artery disease among the diabetics.

This study has clearly shown that all lipid fractions (except HDL-c) are abnormally elevated in diabetes when compared with controls (Table I). Our findings were fell in line with previous studies undertaken.<sup>14,16</sup> These studies had suggested that the lipoprotein distribution in T2D is not significantly altered by the degree of metabolic control.<sup>14,15,16</sup> Realizing that most of the diabetics have a high probability of developing cardiovascular and cerebrovascular disease,<sup>17</sup> it 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.

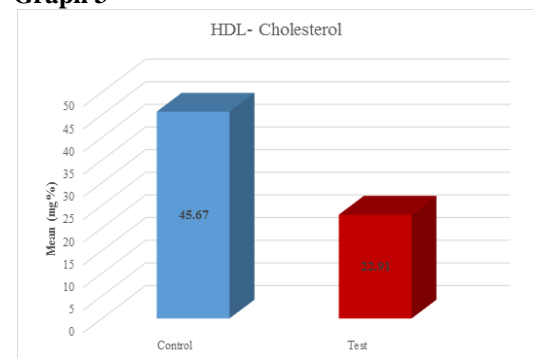
**Graph 1**



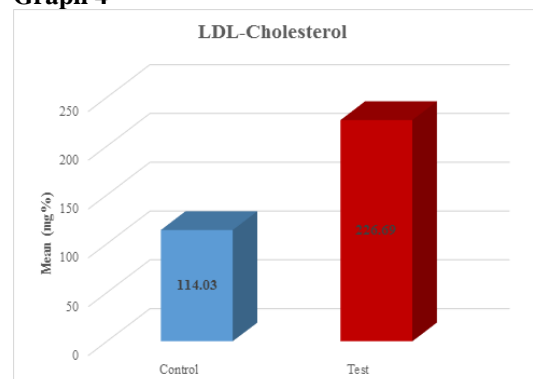
**Graph 2**



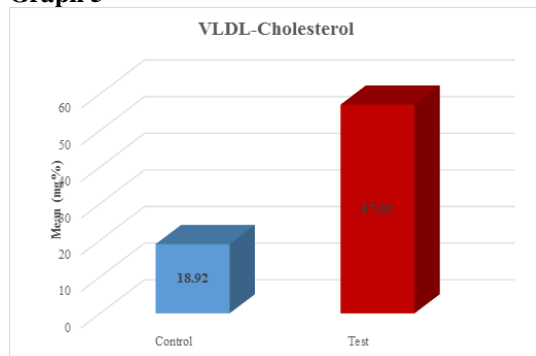
**Graph 3**



**Graph 4**



**Graph 5**



### Conclusion

The study signifies that dyslipidaemia exists in T2D. Therefore, lipid profiling for all persons with type 2 DM should be a routine test. All persons with type 2 diabetes must be started on primary prevention by encouraging healthy lifestyle diets so as to reduce the risk of CHD and atherosclerosis. Further studies should be undertaken to establish the dietary pattern of type 2 diabetic patients and other factors that may lead to hyperlipidemia.

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