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Plasma Cholesterol Profile And Their Internal Ratio In Type-2 Diabetes Mellitus

Nagendra. S[1], Srinivas S[2] & Kashinath R T[3*]

[1](*Associate Professor, Dept of Medicine, Subbaiah Institute of Medical Sciences,NH-13,Purale, Shivamogga-577222,India e-mail:smcshimoga@yahoo.co.in)*
[2](*Assistant Professor, Dept of Dermatology, Subbaiah Institute of Medical Sciences,NH-13,Purale, Shivamogga-577222,India. e-mail:skin.srinivas@yahoo.com)*
[3](*Professor & HOD, Dept of Biochemistry, Subbaiah Institute of Medical Sciences,NH-13,Purale, Shivamogga577222,India e-mails:rsearch.smc@gmail.com & drkashinath_1945@yahoo.co.in)*

Address for Correspondance:*
Dr Kashinath R T
Professor & HOD Subbaiah Institute of Medical Sciences, NH-13, Purale, Shivamogga-577222
Mobile no-9886517959

Abstract:. *Diabetes mellitus induced dyslipidemia is the root cause of life threatening micro and macro vascular complications in type-2 diabetic subjects. The principle predictor of diabetes induced cardio vascular complications which are normally employed are becoming less consistent due to use of various lipid lowering agents. It has been suggested that plasma triacylglycerol levels alone is an independent risk factor of cardio vascular complications in diabetes mellitus. The cholesterol profile and their internal ratios may through much light on prediction of dyslipidemia induced cardio vascular complications in diabetes mellitus. Hence a study was planned to assess the plasma cholesterol profile and their internal reciprocals in type-2 diabetes mellitus.*
A fasting blood sample from both Normal subjects(n=95) and from type-2diabetic subjects(n=132) was collected and was employed for estimation of cholesterol profile as well as triacylglycerol levels.
The results indicate a significant($p<0.001$) fall in the ratio of total cholesterol/VLDL cholesterol in type-2 diabetic subjects of both sexes as compared to normal subjects indicating this ratio is a determinant of diabetes induced dyslipidemia and may be clinically employed as significant predictor of dyslipidemia induced complications in type-2 diabetic subjects.

Keywords:- *Diabetes Mellitus(DM), Total cholesterol(TC),Triacylglycerol(TAG), HDL, VLDL, LDL & TC/VLDL .*

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I. Introduction

Apart from a significant disturbance in glucose metabolism in Type-2 Diabetes Mellitus(T-2DM), which is either due to subnormal amount or subnormal functioning of insulin[1,2], it is known that T-2DM predisposes a gross alterations in lipid metabolism leading to dyslipidemia[3-6]. Previous studies have shown that dyslipidemia in Diabetes Mellitus(DM) is closely associated with insulin resistance and hyperglycemia which in turn increases Reactive Oxygen Species(ROS) together contributing to oxidation of LDL particle leading to atherosclerosis and coronary heart diseases[7,8].

Raised levels of total cholesterol and triacylglycerol in plasma in T-2DM is familiar and is the root cause of diabetic complications including micro and macro vascular complications[9,10,11]. It is known that the plasma levels of HDL cholesterol(HDLC) as well as the ratio of TC/HDLC are the principle predictors of these vascular complications in T-2DM and assist in controlling or delaying such complications.

Triacylglycerols in plasma are normally transported by lipoprotein fractions- Chylomicrons and VLDL, where as the cholesterol is being transported both by LDL and HDL fractions. A detailed study of various lipoprotein fractions and their reciprocals may be beneficial in T-2DM patients in ascertaining their dyslipidemic status. The different lipoprotein fractions can be evaluated by their cholesterol content.
Hence a study was planned to evaluate the significance of these lipoprotein fractions and their internal ratios in T-2DM patients.

II. Materials & Methods

The T-2DM patients aged above 35years of both sexes visiting the medical Out Patient Department (OPD) of Subbaiah Medical College Hospital and Research Centre, Shivamogga for routine check up were randomly selected. A brief history of disease was taken. The normal control subjects were taken from employees of Subbaih Institute of Medical Sciences, Shivamogga, Subbaiah Institute of Dental Sciences, Shivamogga and from the employees of attached hospitals.

A fasting blood sample(5-7 plain blood) with heparin as anticoagulant was collected from normal controls and from diabetic subjects after obtaining an informed consent. The samples were centrifuged at 3600 rpm to separate plasma. The separated plasma samples were employed for the estimation of Total cholesterol(TC)[12],Triacylglycerol(TAG)[13,14], HDL cholesterol(HDLC)[15,16] as well As Fasting Glucose[17] levels. VLDL Cholesterol(VLDLC) and LDL Cholesterol(LDLC) were calculated using Friedwald's formula[18].

1.VLDLC (mg/dl) = TAG / 5

2.LDLC(mg/dl) = (TC – HDLC – VLDLC)

III. Results

The present study includes a total number of 237 subjects having 95 normal subjects , and 132 Type-2 diabetic subjects. Both the normal group and diabetic group were further divided sex wise. The details of the subjects under each category is depicted in Chart-1.

Chart showing the number of subjects normal as well as diabetic subjects in each sub category.

Category	**Number of subjects**
Total number of subjects	**237**
Total number of normal subjects	**95**
Normal Male subjects	**54**
Normal Female subjects	**41**
Total number of T-2DM subjects	**132**
Male T-2DM subjects	**62**
Female T-2DM subjects	**80**

The results observed in the present study are narrated in Table- 1 and Table-2. Table-1 gives the plasma levels of fasting glucose, TC, TAG, HDLC, LDLC, and VLDLC levels inl normal subjects, normal male subjects, normal female subjects, T-2DM subjects, male T2DM subjects and female T-2DM subjects. As seen from the table a significant raise($p<0.001$) is observed in the levels of fasting glucose, TC, TAG and VLDLC in T-2DM Subjects as compared to normal subjects, where as a little fall in HDLC seen in T2DM subjects as compared to normal subjects.

Table-2 narrates levels of fasting glucose and the calculated ratios of TC/HDLC, TC/LDLC, TC/VLDLC, TC/(HDLC+LDLC), TC/(LDLC+VLDLC), TC/(HDLC+VLDLC) levels normal subjects, normal male subjects, normal female subjects, T-2DM subjects, male T-2DM subjects and female T-2DM subjects.It is evident from the table that the calculated ratio TC/HDLC is significantly raised in T-2DM subjects as compared to normal subjects where as TC/VLDLC and TC/(HDLC+VLDLC) ratios are significantly lowered in T-2DM subjects as compared to normal subjects, suggesting that these parameters may be useful in assessing the dyslipidemic status of the T-2DM subjects.

Bar graph-1 gives the comparision TC/HDLC , LDLC/HDLC and TC/VLDLC ratios in normal subjects as well as in T-2DM subjects. It is evident from grach that there is striking decreas in ($p<0.001$) in TC/VLDLC ratio in T-2DM subjects as compared to normal subjects highlighting this ratio may be an useful index in diabetes induced dyslipidemia.

IV. Discussion

Diabetes Mellitus (DM) is a systemic metabolic disease characterized by hyperglycemia , hyperlipidemia, hyperaminoacidemia and hypo-insulinemia that results from both insulin secretion and action[1,2,19]. Dyslipidemia, a complication associated with DM leads, to profound alteration in concentration and composition of lipid profile in the body which leads to increase in lipid concentration in body fluids[20-22]. It is known that in DM the levels of total lipids, specifically triacylglycerols (TAG) and total Cholesterol (TC) are increased in both plasma and tissues significantly[20]. Diabetic dyslipidemia may result in many micro and macro vascular complications including retinopathy, nephropathy and neuropathy[9-11,21-22]. Normally diabetic dyslipidemia increases in fasting serum TAG levels with decreased HDLC levels as well as an increased LDLC levels [23,24]. It is proposed that in DM long term hyperglyeima causes generalized vascular endothelial damage thereby reducing functional lipoprotein lipase leading to an increase in TAG and decrease in

HDLC. This scenario leads to increased levels of VLDLC, TAG and LDLC thus results in precipitation as well as progression of atherosclerosis[25].TC/HDLC and LDLC /HDLC are employed to predict coronary disease in DM[26-28]. The significant raise observed in the present studies in TC and TAG levels in T2DM subjects as compared to normal subjects in agreement with earlier reports[3,5,8]. It has been suggested by some research workers that TAG itself is an independent risk factor of CVD[29,30]. VLDLC is predominantly depend on TAG levels hence VLDLC may be a strong predictor of CVD in T2DM subjects.

Several lipid ratios have been suggested as simple clinical indicators due to their integrative information of the multiple variables and are strong indicators of cardiovascular risk by their expressions of imbalance between protective as well as atherogenic lipid parameters(31,32). Indeed TC/HDL and LDL/HDL ratios have been shown as two components which are in use to monitor cardiovascular complications in T2DM subjects(33). The present study has thrown light on the strong connections of other lipid ratios, such as TC/VLDL , TC/HDL+LDL and TC/(LDL+VLDL) as positive indicators of cardiovascular risk parameters as compared to known risk factors like TC/HDLC and LDL/HDLC ratios.

The alterations in the common CVD predictors TC/HDLC and LDLC/HDLC in the present study is not that striking hence may not b strong predictor of CVD. Further it is evident from the bar graph that TC/VLDLC shows a significant ($p<0.001$) fall in T2DM subjects as compared to normal subjects suggesting its utility as a strong predictor of dyslipidemia in T2Dm subjects.

A significant alteration observed in TC/VLDLC ($p<0.001$), TC/HDLC+LDLC ($p<0.001$) and in TC/(LDLC+VLDLC) ($p<0.001$) in T2DM subjects strongly suggests the clinical utility of these ratios in assessing the dyslipidemic status of T2DM subjects. However no much variation or significant alterations are observed in these ratios in male T2DM subjects as compared to female T2DM subjects(refer Table-2) suggesting no significant influence of sex hormones on these ratios.

A further study with larger sample size as well as influence and implications of other factors like duration of the disease, type of medication and life style may through sufficient light on efficacy as well as uility of these ratios to assess and to monitor dyslipidemic status in T2DM subjects.

V. Figures And Tables

Table-1

Table-1 gives the plasma levels of fasting glucose, TC, TAG, triacylglycerols, HDL cholesterol, LDL cholesterol and VLDL cholesterol levels levels in normal male subjects, normal female subjects, diabetic male subjects and diabetic female subjects..

Groups ⇨ / **Parameters** ⇩	Normal Subjects			Diabetic Subjects		
	Total (95)	Male (54)	Female (41)	Total (132)	Male (62)	Female (80)
Fasting Plasma Glucose(mg/dl)	94.17 ± 12.98	95.75 ± 15.75	92.66 ± 9.93	141.46*** ± 60.36	151.94*** ± 81.01	133.50*** ± 56.03
Total Cholesterol (mg/dl)	175.24 ± 33.11	174.24 ± 31.70	176.30 ± 34.96	199.00*** ± 59.59	174.81 ± 49.39	217.38*** ± 61.40
Triacylglycerol (mg/dl)	115.04 ± 64.14	120.58 ± 76.98	109.78 ± 50.92	215.50*** ± 130.04	221.28*** ± 109.37	211.76*** ± 146.44
HDL (mg/dl)	59.92 ± 15.59	46.75 ± 17.09	62.93 ± 17.57	54.62* ± 22.20	45.98 ± 17.98	61.18 ± 23.16
LDL (mg/dl)	91.31 ± 46.39	93.60 ± 35.75	89.11 ± 33.78	98.62** ± 39.25	84.63 ± 33.25	139.10*** ± 50.85
VLDL (mg/dl)	24.07 ±	23.87 ±	24.25 ±	45.69*** ±	44.11*** ±	46.89*** ±

	14.54	15.45	13.86	26.02	21.94	29.18

Note:
1. Number in parenthesis indicate the number of subjects
2. The values are expressed as their mean ± SD
3. Statistical evaluation-probability level* p< 0.05, ** p<0.01, *** p< 0.001.

Table-2

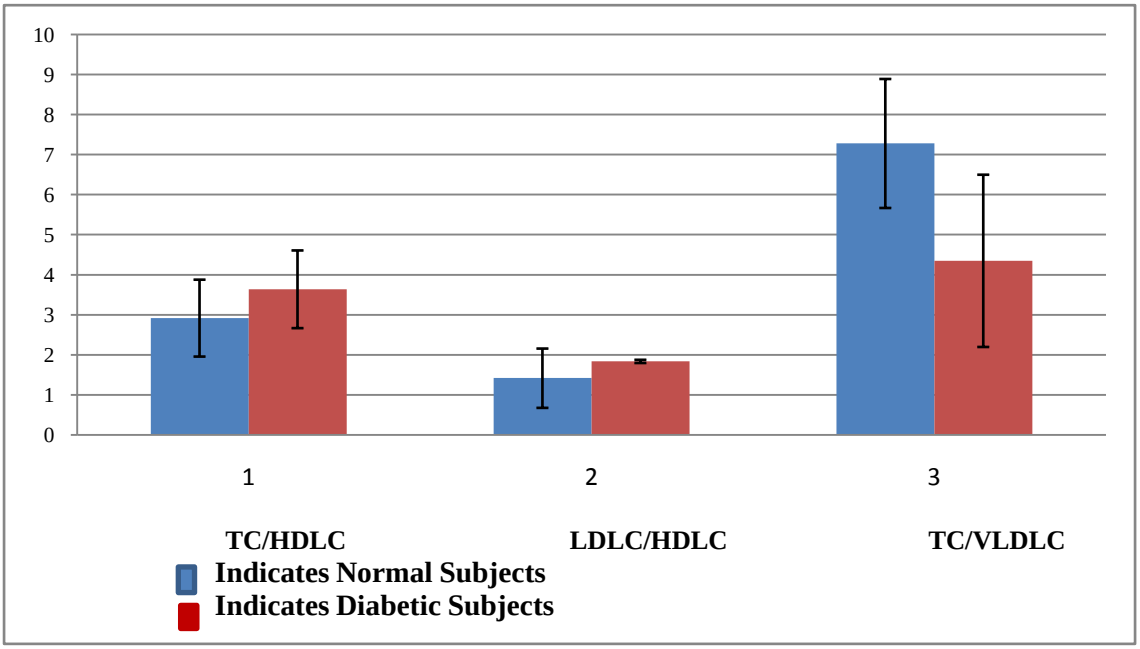
Table-2 depicts the plasma levels of calculated ratios of TC/HDL,TC/LDL,TC/VLDL, TC/HDL+LDL and TC/LDL+VLDL levels in normal males, diabetic males , normal females and diabetic females.

Groups ⇨ / ⇩ **Parameters**	Normal Subjects			Diabetic Subjects		
	Total (95)	Male (54)	Female (41)	Total (132)	Male (62)	Female (80)
TC/HDL C	2.92 ± 0.96	3.72 ± 1.04	2.80 ± 0.89	3.64*** ± 0.97	3.80 ± 0.91	3.55*** ± 1.05
TC/LDLC	1.92 ± 1.09	1.86 ± 0.80	1.97 ± 1.05	2.01 ± 0.58	2.06 ± 0.65	1.56** ± 0.67
TC/VLDLC	7.28 ± 1.61	7.29 ± 0.94	7.27 ± 1.37	4.35*** ± 2.15	3.98*** ± 2.09	4.63*** ± 2.17
LDLC/HDLC	1.42 ± 0.74	2,.08 ± 0.61	1.26 ± 0.88	1.84*** ± 0.04	1.84** ± 0.03	1.67** ± 0.84
TC/HDLC+LDLC	1.15 ± 0.75	1.24 ± 1.22	1.15 ± 0.20	1.29* ± 0.19	1.33 ± 0.22	1.08* ± 0.17
TC/LDLC+VLDL C	1.51 ± 0.28	1.42 ± 1.20	1.55 ± 0.30	1.38*** ± 0.17	1.35 ± 0.10	1.16*** ± 0.21
TC/HDLC+VLDLC	1.90 ± 0.72	1.67± 0.74	1.93± 0.71	1.50*** ± 0.82	1.46 ± 0.79	1.58* ± 0.81

Note:
1. Number in parenthesis indicate the number of subjects
2. The values are expressed as their mean ± SD
3. Statistical evaluation-probability level* p< 0.05, ** p<0.01, *** p< 0.001.

Bar Graph-1

Bar graph showing the of TC/HDLC, LDLC/HDLC and TC/VLDLC ratios in normal subjects and in T2DM subjects.



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