

Significance of plasma total cholesterol-VLDL cholesterol ratio (TC/VLDLC) in Type-2 diabetes mellitus

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Abstract

Dyslipidemia is a significant predisposing factor of diabetes mellitus induced cardio vascular complications in Type-2 Diabetes mellitus (T2DM) subjects. Triacylglycerols and Cholesterol along with phospholipids forms the basic components of tissue lipids and alterations either in their formation or in their composition leads to dyslipidemia. VLDL transports most of the endogenous triacylglycerols. This study was undertaken to assess the significance of plasma total cholesterol- VLDLC ratio (TC/VLDLC) in assessing dyslipidemic status of T2DM subjects as well as to compare the utility of this ratio with known cardio vascular disease markers like Atherogenic Coefficient and Atherogenic Index of Plasma.

T-2DM subjects in the age group of 35-65 years attending Medicine OPD, Subbaiah Medical College Hospital and Research center, Shivamogga for routine check-up were randomly selected. A fasting heparinised blood sample was collected from normal control subjects as well as T-2DM subjects. The samples were centrifuged, separated plasma employed for estimation of Total Cholesterol, Triacylglycerol, HDL-Cholesterol and fasting glucose levels. VLDL Cholesterol, Atherogenic Coefficient (AC), Atherogenic Index of Plasma (AIP) and TC/VLDLC ratio calculated.

A significant raise($p < 0.001$) is observed in levels of fasting glucose, TC, TAG, VLDLC, AC, and AIP in T2DM subjects as compared to normal control subjects where as a significant fall is seen in the calculated values of TC/VLDLC ratio. Hence it can be concluded that along with AC and AIP the TC/VLDLC ratio is a valuable additional marker of diabetes induced dyslipidemia suggesting its clinical utility in assessing and prevention of dyslipidemia induced cardio vascular complications in T2DM subjects.

Keywords: Total cholesterol, Triacylglycerol, AC, AIP.

1. Introduction

Diabetes Mellitus (DM) is a multi-systemic disorder characterized by hyperglycemia, hypelipidemia and micro or macro vascular complications [1-3]. The significant pre-disposing factor of diabetes mellitus induced vascular complications is “dyslipidemia”, an alteration in the composition and in concentration of lipids in the body [4-9]. The basic components of the body lipids are triacylglycerols, cholesterol and phospholipid and the metabolism of triacylglycerols as well as cholesterol is much affected in diabetes mellitus due to the abnormal raise in the availability of precursor substrates like acetyl CoA, Fatty acids and glycerol-phosphate[10-13] resulting in

increased formation of basic lipid components leading to dyslipidemia. Endogenous triacylglycerols are principally transported in blood plasma by VLDL particles which are also involved in formation of LDL-particles suggesting that VLDL may be an interesting and important predictor of diabetes mellitus induced dyslipidemia. Hence this study was undertaken to assess the significance of plasma total cholesterol- VLDL cholesterol (TC/VLDL) ratio in type-2 DM as well as to correlate this ratio with atherogenic index of plasma (AIP) and Atherogenic Coefficient (AC), the known predictor of cardiovascular disease (CVD).

T-2DM subjects in the age group of 35-65 years of both sexes registered at the medical OPD of Subbaiah Medical College Hospital and Research center, Shivamogga for routine check-up were randomly selected. Normal control subjects in the same age group belonging to both sexes were taken from employees of Subbaiah Institute of Medical Sciences, Shivamogga, Subbaiah Institute of Dental Sciences, Shivamogga and from the employees of attached hospitals.

2. Materials & Methods

Fasting heparinised blood sample (5-7ml) was collected from normal control subjects as well as T-2DM diabetic subjects after obtaining an approval by Institutional Ethics Committee (Ref. No: SUIMS/R&D/IEC/006/2017). The samples were centrifuged at 3600 rpm to separate plasma. The separated plasma sample was employed for the estimation of Total Cholesterol (TC) [14], Triacylglycerol (TAG) [15,16], HDL-Cholesterol(HDLC)[17,18] as well as fasting glucose levels[19]. LDL Cholesterol (LDLC), VLDL Cholesterol (VLDLC), Atherogenic Coefficient (AC), Atherogenic Index of Plasma (AIP) and TC/VLDLC ratio were calculated using the following established relationships [20-22].

1. $VLDLC = (TAG/5)$
2. $LDLC = (TC - HDLC - TAG/5)$
3. $AC = (TC - HDLC / HDLC)$
4. $AIP = \log (TAG / HDLC)$

2.1 Statistical Analysis

Data are expressed as their Mean \pm SD. The statistical significance was assessed by Student 't' test. $p < 0.05$ is considered statistically significant.

3. Results

A total number of 237 subjects were chosen for the present study which included 95 normal subjects and 142 T2DM subjects. The T2DM subjects who are being treated for various endocrine disorders are excluded from the study. Both the normal subjects as well as T2DM subjects were further sub grouped into sex. The details of the number of subjects in each group and sub group are narrated in Table 1.

Table 1: Chart showing the number of normal subjects as well as T2DM subjects in each group and sub group

Total number of subjects	237
Total number of normal subjects(Group-N)	95
Normal Male subjects(Group-N ₁)	54
Normal Female subjects(Group-N ₂)	41
Total number of T-2DM subjects(Group-D)	142
Male T-2DM subjects(Group-D ₁)	62
Female T-2DM subjects(Group-D ₂)	80

The results of the present study are given in Table-1 as well as in Bar graph-1. Table-1 shows the plasma levels of glucose, TC, TAG, HDLC, LDLC, VLDLC, AC, AIP and TC/VLDLC ratio in normal subjects (Group-N),

normal male subjects(Group-N₁), normal female subjects (Group-N₂), T2DM subjects (Group-D), male T2DM subjects (Group-D₁) and female T2DM subjects (Group-D₂). It is seen from the table that a significant raise is observed in levels of fasting glucose, TC, TAG, VLDLC, AC, and AIP in T2DM subjects as compared to normal control subjects where as a significant fall is seen in the calculated values of TC/VLDLC ratio. The difference observed between Group-N₁ and Group-N₂ as well as Group-D₁ and Group-D₂ specifically in Atherogenic Coefficient (AC) and Atherogenic Index of Plasma (AIP) levels may be due to the hormonal effects as it is known that estrogen is having a significant effect on lipid metabolism/turnover.

Figure 1 showing the comparison of the levels of AC, AIP and TC/VLDLC ratio in control subjects (Group-N) as well as in T2DM subjects (Group-D). It is evident from the graphs that there is a parallel alteration in TC/VLDLC ratio as compared to the alterations seen in AC and AIP levels in Group-N and Group-D subjects suggesting usefulness of TC/VLDLC ratio in T2DM subjects in assessing dyslipidemia.

4. Discussion

Dyslipidemia, a principle predisposing condition of cardiovascular risk is characterized by elevated triacylglycerols, Cholesterol and the related lipoprotein fractions [23].

T2DM subjects are the more vulnerable group for the risk of developing cardiovascular diseases due to an underlying dyslipidemia resulting from gross alteration in the fat metabolism in these subjects. No doubt there exist an independent relationship between HDLC and cardiovascular risk, the contribution of triacylglycerols cardiovascular risk cannot be neglected. The triacylglycerols, cholesterol and lipo-proteins are implicated in the pathogenesis of Coronary artery diseases especially Atherosclerosis [24,25]. Increased LDL, decreased HDL and increased triacylglycerols have been shown to be responsible for the pathogenesis of atherosclerotic lesions [26]. Recently Atherogenic Coefficient (AC) as well as Atherogenic Index of Plasma (AIP) has been employed to predict cardiovascular diseases (CVD).

The triacylglycerols and the cholesterol are two important lipids constituent that make up the lipoproteins, the principle lipid transporting particles in human system. The endogenous or liver synthesized triacylglycerols are principally transported by lipoprotein VLDL, where as cholesterol being transported by both LDL and HDL lipoprotein fractions, further the LDL arises from VLDL fraction. Thus it becomes significant in dyslipidemia the composition of these two principally alters and might be significant.

It is observed in the present study that there is a significant raise in plasma triacylglycerols as well as in plasma total cholesterol levels in T2DM subjects as compared to control subjects suggesting that dyslipidemia observed in these T2DM subjects is due to raise in Triacylglycerols and cholesterol levels or to alterations in lipoprotein fractions involved in their transport. This is in agreement with many earlier reports [6,8,9]. And this abnormality may not be due to hyperglycemia but probably may be due to insulin resistance [27].

Cardiovascular complications including atherosclerosis is a multi factorial process, but abnormalities in plasma as well as dyslipidemia are one of the major key factors in development of cardiovascular complications [28].

The development of CVD is normally predicted by many atherogenic indices and the most generally employed are : Atherogenic Coefficient(AC) and Atherogenic Index of Plasma(AIP) as the dyslipidemia is

the major factor in T2DM subjects and because the increase in triacylglycerols as well as cholesterol are principle contributors for diabetic dyslipidemia, the ratio of TC/VLDLC is being assessed in the present study and is compared with the known Cardio vascular disease(CVD) predictors- AC and AIP[21,22]. Along with a raise in AC and AIP in T2DM subjects of both sexes we observed in the present study a significant fall ($p < 0.05$) in TC/VLDLC ratio in Group-D subjects as compared to Group N subjects (Table 1, Figure 1).

5. Conclusion

It can be concluded from the present study in T2DM subjects that along with AC and AIP the TC/VLDLC ratio is a valuable additional marker of diabetes induced dyslipidemia suggesting its clinical utility in assessing and prevention of dyslipidemia induced cardiovascular complications in T2DM subjects.

Table 1: Plasma levels of biochemical parameters

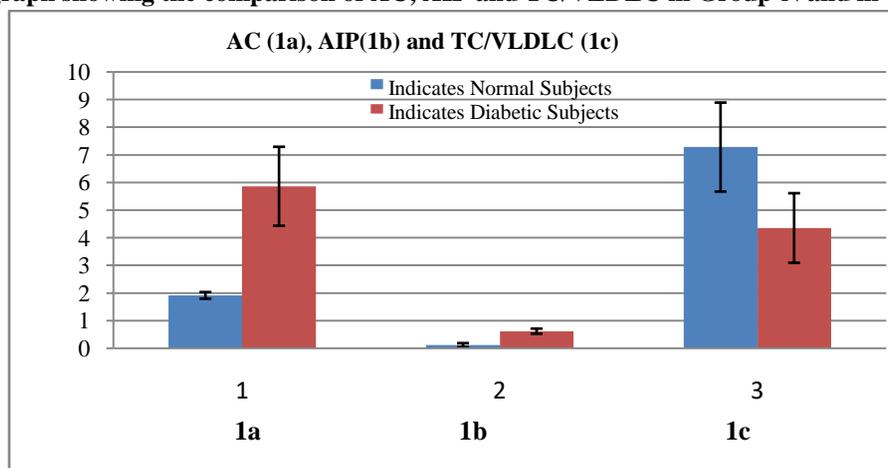
Parameters Groups	Glucose (mg/dl)	TC (mg/dl)	TAG (mg/dl)	HDLC (mg/dl)	LDLC (mg/dl)	VLDLC (mg/dl)	AC	AIP	TC/VLDLC
Group N	94.17± 12.98	175.24± 23.11	110.04± 34.14	59.92± 9.59	91.31± 46.39	22.07± 5.12	1.91± 0.12	0.114± 0.068	7.28± 1.61
Group N1	75.70± 12.90	174.12± 24.90	120.58± 21.48	56.75± 15.08	93.60± 35.75	23.37± 8.80	1.72± 0.09	0.109± 0.080	7.29± 1.32
Group N2	72.60± 13.60	176.30± 26.30	109.70± 22.90	62.93± 17.57	89.11± 33.78	24.65± 9.20	2.01± 0.65	0.168± 0.078	6.88± 1.21
Group D	151.46 ^{***} ± 20.36	229.00 ^{***} ± 29.59	215.50 ^{***} ± 41.28	34.62 ^{***} ± 8.26	98.62 ^{**} ± 39.25	43.10 ^{***} ± 12.28	5.86 ^{***} ± 1.43	0.615 ^{***} ± 0.093	4.35 ^{***} ± 1.26
Group D1	152.31 ^{***} ± 23.80	217.35 ^{***} ± 31.20	221.75 ^{***} ± 36.40	39.90 ^{***} ± 16.92	84.63± 33.25	44.89 ^{***} ± 9.18	6.54 ^{***} ± 1.12	0.528 ^{***} ± 0.088	3.98 ^{***} ± 1.21
Group D2	132.60± 18.90	208.80 ^{***} ± 22.20	210.80 ^{***} ± 22.60	38.42 ^{***} ± 13.50	139.10 ^{***} ± 50.85	43.60 ^{***} ± 8.12	7.42 ^{***} ± 1.43	0.660 ^{***} ± 0.094	4.60 ^{***} ± 1.17

Note: 1) Number in parenthesis indicates the number of subjects in that group; 2) Values are expressed as mean ± SD; 3) Statistical evaluation-probability level * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Table showing the plasma levels of total cholesterol (TC), HDL Cholesterol(HDLC), LDL Cholesterol (LDLC), VLDL Cholesterol (VLDLC), Triacylglycerol (TAG), as well as calculated values of atherogenic coefficient (AC), atherogenic index of plasma

(AIP) and TG/VLDLC in normal control subjects (Group-1), normal control male subjects (Group N1), normal control female subjects (Group N2), T2DM subjects (Group D), male T2DM subjects (Group D1) and in female T2DM subjects (Group D2).

Figure 1: Bar graph showing the comparison of AC, AIP and TC/VLDLC in Group-N and in Group-D subjects



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