FBG AND TC/HDL RATIOS IN TYPE 2 DIABETES MELLITUS

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Background: Presence of dyslipidemia. i.e. raised Total Cholesterol (TC) and decreased High Density Lipoproteins (HDL) is an established phenomenon in type 2 diabetes mellitus. Its relationship to the fasting blood sugar (FBG) level in both diabetics and non-diabetics has yet to be established. The present study aims to show such a relationship. ***Methods***: 150 subjects were selected and divided into two groups, one of 50 controls (non-diabetics), the other of 100 patients with type 2 diabetes mellitus. Their FBG levels were determined by enzyme oxidase method, and their TC and HDL levels were determined using a standard kit method. ***Results:*** FBG and TC: HDL ratios were increased in the patient group ($p = <0.001$). Comparison of FBG and TC: HDL ratios revealed a highly significant rise ($p = <0.001$) in the patient group. FBG with TC: HDL ratios between both groups showed a positive correlation ($r = 0.554$). ***Conclusion:*** The results of the present study suggest an association between FBG and TC: HDL ratios, which may be a contributory factor to the increased prevalence of coronary artery disease in patients with type 2 diabetes mellitus.

INTRODUCTION:

Diabetes mellitus (DM) is a metabolic syndrome characterized by hyperglycemia due to an absolute or relative deficiency of insulin or an increased end-organ receptor resistance to the effects of normal or raised insulin levels, or both.[12] The altered metabolic pattern and lack of insulin effect leads to a cascade of events that further result in dyslipidemia and abnormal protein end products (glycated proteins and amino acids). Both these events are believed to predispose to the higher prevalence of cardiovascular disease in T2DM patients.

Cardiovascular disease is the leading cause of morbidity and mortality in patients with uncontrolled type 2 diabetes mellitus (T2DM). Coronary Artery Disease (CAD) accounts for 70% of the mortality in these cases. [3] Moreover dyslipidemia is also common among these patients.[4,5,6] TC levels have been targeted as the single most important factor in causing atherosclerosis, CAD and perhaps even diabetic microangiopathy.[7, 8] The association between DM and cardiac disease is complex. Hypertension, hypercholesterolemia and hypertriglyceridemia are all more common in diabetics. Patients with poorly controlled DM exhibit a significantly increased mortality with CAD.[2,7,9] Another study shows that the mortality rates from CAD in T2DM are 3-6 times higher than in nondiabetics.[4]

Poorly or inadequately controlled T2DM patients are the ones most prone to cardiovascular morbidity and mortality. The lipid profile in T2DM patients is characterized by raised serum Triglyceride (TG) and TC, and reduced HDL cholesterol (HDL- C). Low Density Lipoprotein (LDL) and LDC

cholesterol (LDL-C) are raised but show the same distribution as that of non-diabetic dyslipidemics[8]. Another study on risk factors for CAD in T2DM indicated the importance of raised LDL-C, decreased HDL, increased TG, HbA^, and FBG.[7]

TC/HDL ratio is important in indicating the risk of CAD in T2DM patients. Ratios > 4.5 are dangerous, while optimal ratios are around 3.5.[4,1] The TC: HDL ratio estimates the net effect of the two- way traffic of cholesterol in and out of tissues, and presumably also the vessel wall. [4,11] It has therefore been suggested as the most powerful predictor of premature or accelerated development of CAD in T2DM patients.[12]

This study was undertaken to determine any possible correlation between FBG and TC: HDL ratio in patients with T2DM. Objectives of the study were a) to demonstrate dyslipidemia in T2DM patients b) to determine a significant increase in TC: HDL ratios in T2DM patients and to show it to be a risk factor for CAD.

MATERIALS AND METHODS:

The study was conducted at Pakistan Medical Research Centre (PMRC) Laboratories at Peshawar and Abbottabad, Department of Chemistry' University of Peshawar, Departments of Biochemistry and Pathology of Ayub Medical College Abbottabad. The time period of the study was from April 1998 to October 2000.

100 patients with T2DM and 50 nondiabetic controls ranging in ages from 35 - 65 years were included in the study. They were divided into Group 1 (Controls) and Group 2 (Patients). Relevant history of present disease and presence or absence of cardiac (CAD) disease was obtained on performas, 5 ml of venous blood samples were taken from all subjects after an overnight fast of 12 hours. 1.5 ml aliquot of anticoagulated blood was used for determining FBG by enzymatic oxidase method. 3.5 ml aliquot was allowed to clot, the serum separated, and used to determine serum TC and HDL levels by kit methods (Randox TC and HDL kits).

Data was entered into SPSS 8.0 computer program for statistical analysis. Statistical analysis was done using z-tests, student's t-test and chi-square tests, as

applicable. Spearman's Rank Correlation and Regression Analyses were also performed.

RESULTS:

The results of the study are given in Tables 1 - 4 and Figure 1.

Table - 1: Mean FBG, TC/HDL levels in controls and patients

GROUPS	STATISTICS	FBG mg/dl	TC mg/dl	HDL mg/dl
CONTROLS (N = 50)	MEAN + SD	84 3400 11.9123	201.06 23 3312	47.72 5 7394
PATIENTS (N = 100)	MEAN + S.D.	143.16 33.2428	273.7 50.129	41 2900 7.3255
	P VALUE	< 0.001	< 0.001	<0 001

Table - 2: Correlation of FBG and TC/HDL ratios in controls

FBG		TC :HDL RATIOS				TOTALS	r VALUE
mg/dL	-3	5.1	7.1	91	11+		
	5	-7	-9	-11			
70-80	27	2	-	-	-	29	0 187
81 -90	4	2	-	-	-	6	0.554
91 - 100	11	1	-	-	-	12	0.451
101 - no	2	1	-	-	-	3	0 602
TOTALS	44	6				50	

Table – 3: Correlation of FBG and TC/HDL ratios in patients

FBG mg/dL		TC: HDL RATIOS				TOTALS	r VALUE
	3-	5.1	7.1	91	11+		
	5	-7	-9	-II			
90- 120	6	7	4	~	-	17	0 005
121 - 150	8	14	25	II	1	59	0 553
151 - 180	6	2	3	1	-	12	422
181 - 210	3	1	1	2	-	7	231
211 -240	—	-	1	1		2	0 676
241 - 280	1	1	1	-	-	3	
TOTALS	24	25	35	15	1	100	

The data indicate a highly significant difference between the mean values of FBG, TC and HDL between controls and patients (p = <0.001) (Table - I). The FBG and TC.'HDL ratios in patients were significantly raised (p <0.001) (Table - 2). FBG showed a direct correlation with the TC: HDL ratios in both groups (control r = +0.55, patient r = + 0.5). (Table - 3).

The correlation of FBG and TC: HDL ratios plotted for all 150 subjects showed a significant value by Spearman Rank Correlation test (r 0.559) (Figurc-1).

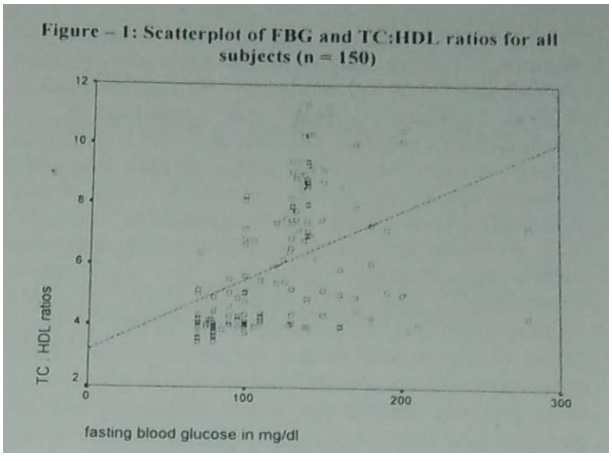

Table - 4: History of cardiovascular disease in controls and patients

Groups	Hypertension	History of angina	History of Ml	Angina plus Ml
Controls (N = 50)	12(24%)	7(14%)	6(12%)	4 (8%)
Patients (N = 100)	37 (37%)	59(59%)	35 (35%)	34 (34%) 1
P Values	<0 001	<0 001	< 0 001	<0 001

It is obvious from Table - 4 that there is a highly significant difference in the frequencies of cardiovascular diseases between controls and patients; moreover, CAD related events feature prominently in the patient group.

DISCUSSION:

Our results indicate a significantly raised difference of values of FBG, TC and TC: HDL ratios between controls and patients. This indicates that dyslipidemia is an important part of the disturbed metabolic milieu of the T2DM patient. Furthermore, the type of dyslipidemia is relevant to the accelerated atherosclerotic and CAD events found in these patients. Our study also shows that there is a significantly higher frequency of CAD and related events in T2DM patients.

There is no doubt of the propensity of T2DM to cause a serious increase in morbidity and mortality associated with CAD. It is of course tempting to link the increased prevalence of CAD with the dyslipidemia profile found in increased frequency in these patients. Several studies have been able to show such a relationship. [4,8] However other studies including the present one have consistently shown a lack of correlation between these two variables. In

fact, in our study there was a significant negative correlation between TC.HDL ratios and various types of CAD (Pearson and Spearman correlation values from -0.2 to 0.3, p 0.05 to 0.01). It appears that what holds true for non- diabetic dyslipidemia is not a valid (or at least statistically valid) assumption for the dyslipidemia of T2DM patients. Thus the contribution of dyslipidemia towards CAD in T2DM patients remains a moot issue, stimulating research into other possible causes of the increased CAD and related morbidity and mortality in these patients.

It is pertinent to note that lipid lowering regimens which are routinely employed for non-diabetic dyslipidemia have little place in correcting CAD related morbidity and mortality in T2DM patients. Many treatment and follow up protocols for T2DM patients do not even monitor the lipid profiles of these patients, despite the known propensity towards dyslipidemia and CAD related events (Grover). This practice may have its base in the statistically unproved hypothesis of dyslipidemia contribution to CAD in these patients. Nevertheless, the monitoring of all possible risk factors in the causation of CAD is a practice to be upheld till definite proof is forthcoming or the real risk factor(s) identified.

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