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Short Communication

Evaluation of gamma glutamyl transferase as a marker of cardiovascular risk, in 200 angiographically proven coronary artery disease patients

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ABSTRACT

Gamma glutamyl transferase (GGT) is emerging as a promising marker for assessing cardiovascular risk. GGT predicts cardiovascular mortality in the population and is positively associated with traditional risk factors for coronary artery disease (CAD). This study was undertaken on 200 north Indian CAD patients diagnosed with coronary angiography to study relation of GGT with risk factors for CAD and severity of CAD. GGT values ranged from 5 to 69U/L and were divided in 4 quartiles. GGT was positively associated with triglyceride ($p = 0.008$) and VLDL cholesterol ($p = 0.002$) in our subjects. Also an increase in total cholesterol from GGT quartile I to quartile IV ($p = 0.28$) was noted.

1. Introduction

The search for novel risk factors to explain inter-individual variation in cardiovascular risk continues. Oxidative stress, either in the form of free radicals or via modification of LDL, has an integral role in the initiation and progression of atherosclerosis. GGT is a sensitive indicator of hepatic diseases and excessive alcohol consumption. Its role in metabolism of glutathione, a major antioxidant, has also been demonstrated. GGT is involved in generation of free radicals in the extracellular space, leading to oxidation of LDL.[1] Catalytically active GGT has been found within atherosclerotic coronary plaques.[2] GGT is a promising biomarker of oxidative stress and cardiovascular risk assessment. Data on GGT in Indian population is scarce,[3,4] hence we evaluated 200 north Indian established CAD patients and correlated GGT levels with risk factors and severity of CAD.

2. Materials and methods

Two hundred consecutive patients, undergoing coronary angiography or therapeutic coronary artery intervention procedure were enrolled after giving an informed written consent. Patients with liver disease, renal failure, active infections, malignancies or active alcohol consumption were excluded. Anthropometric measurements, blood pressure were recorded. Blood samples were collected prior to intervention, after overnight fasting. GGT, blood glucose, renal function tests and liver function tests were performed on Randox make, Imola model Clinical Chemistry Analyser. Diabetes mellitus, hypertension, obesity, Metabolic Syndrome and dyslipidemia were defined by routine criteria. Details of angiographic evaluation were noted from records. Participants were divided in 4 groups according to GGT quartiles. Prevalence of atherosclerotic risk factors in different GGT quartiles were compared between quartiles using Student's *t*-test, p value of <0.05 was considered significant. The research protocol was approved by the institutional ethics committee.

3. Results

Study population was composed of 167 (83.5%) males (28–80 years, mean 56.2 years) and 33 (16.5%) females (38–75 years, mean

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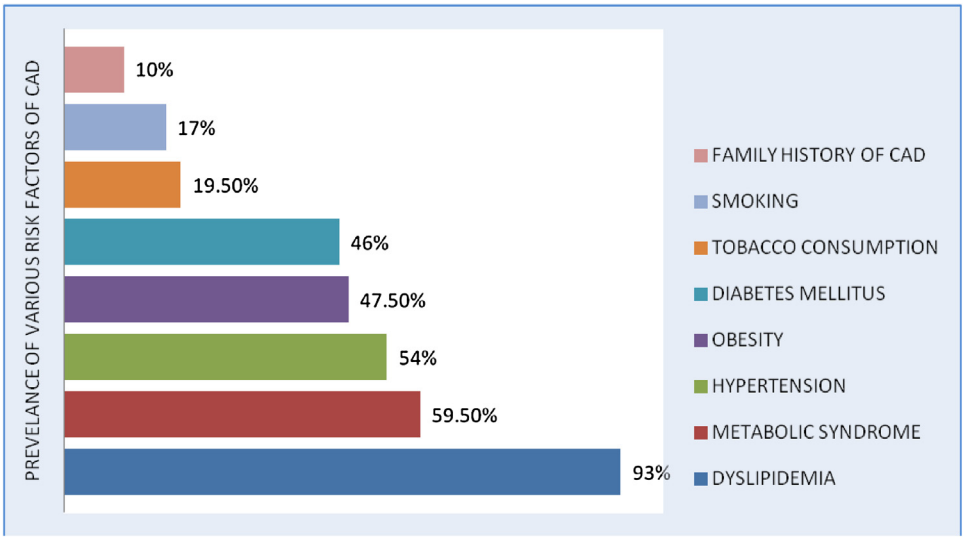

Fig. 1. Prevalence of various risk factors in the cohort. Most prevalent atherosclerotic risk factor was dyslipidemia, followed by metabolic syndrome and hypertension.

56.2 years). Most prevalent cardiovascular risk factor was dyslipidemia, seen in 93% patients. Most common abnormality was low HDL seen in 88.5% patients (18–82 mg/dl, mean 32.1 mg/dl). Prevalence of other risk factors is shown in Fig. 1.

GGT values ranged from 5 to 69U/L in males (mean 29.2 U/L) and 8 to 50U/L (mean 26.3 U/L) in females (p = ns). Table 1 depicts GGT quartiles.

Mean triglyceride and VLDL values showed a rising trend from quartile I to IV and the difference in levels between quartile I and quartile IV was statistically significant (p = 0.008, 0.002 respectively). A rise in total cholesterol values was seen from quartile I to quartile IV (p = ns). No trend was observed in LDL and HDL cholesterol across various GGT quartiles. In other risk factors, mean waist circumference increased from GGT quartile I to quartile IV (p = ns).

On angiography the most common finding was single vessel disease (29%) followed by triple vessel and left main coronary artery disease (28%). Patients with the most severe form of coronary vessel involvement i.e. triple vessel and left main coronary artery disease were maximum in quartile IV and they increased from quartile I to quartile IV (15%–38%). Further the mean GGT value was lowest in those with normal coronaries and mild CAD and there was a rising trend in the GGT values with increasing disease severity (p = ns).

No trends were observed across GGT quartiles for prevalence of other risk factors evaluated. Quartile III had the highest mean BMI and maximum prevalence of hypertension, diabetes and obesity.

Table 1
GGT quartiles: The table represents the 4 GGT quartiles with number of patients in each quartile.

	Number of Patients (n)	Range (U/L)	Mean (U/L)	SD
Quartile I	48	5–16	12.4	2.6
Quartile II	52	17–24	20.3	2.3
Quartile III	50	25–39	30.9	4.2
Quartile IV	50	≥40	50.8	9.6

4. Discussion

GGT levels are strongly associated with all-cause mortality and deaths from ischemic heart disease.[5] Population based data show a positive association of GGT and traditional cardiovascular risk factors including old age, male gender, BMI, smoking, lack of exercise, hypertension, hypercholestrolemia, hypertryglyceridemia, low HDL and high fasting glucose.[6] These relationships are strong even with normal GGT levels. Also baseline GGT is an independent risk factor for the development of heart disease, hypertension and type 2 diabetes, regardless of alcohol consumption.[7,8] In addition, elevated GGT levels show a positive correlation with Framingham cardiovascular risk scores of non-diabetic, non-obese adults.[9] Increased liver fat and carotid intima-media thickness, both indicative of atherosclerosis, are shown to be associated with normal or slightly elevated GGT levels.[10] The role of GGT in glutathione regulation and degradation and generation of oxidative stress is well established.[11]

In our study we selected patients who underwent coronary intervention and evaluated their risk factor profile along with GGT levels. The sample had predominance of males. Mean age was 56.2 years with 62% participants below 60 years of age. This is in conjunction with the observation that CAD in Indians develops 5–10 years earlier than other ethnic groups.

Prevalence of risk factors including dyslipidemia, hypertension, diabetes, metabolic syndrome and abnormal BMI were comparable to cohorts of CAD patients from various parts of the country.[12,13]

Mean GGT value was 28.7U/L, higher in males (29.2U/L) than females (26.3U/L), this is within the normal reference range. Study on a similar cohort showed comparable GGT values.[14] GGT levels in quartiles were compared to risk factors, and a significant association was found with triglyceride (p = 0.008) and VLDL cholesterol (p = 0.002). A smaller sample size of our study could explain the lack of relation between LDL and GGT in the data.

Mean GGT was higher in those with multivessel and left main disease compared with normal coronaries or mild CAD (32.4U/L vs 24.7U/L, p = 0.66). A study of 237 patients of ACS showed significantly higher GGT levels in patients with significant coronary artery stenosis vs those without.[15] Aksakal et al., demonstrated an increase in GGT levels from low SYNTAX tertile to high tertile in 442 patients with stable angina pectoris who

underwent coronary angiography.[16] Association of GGT with other risk factors was not demonstrated in our cohort.

Limitations of the study include a small sample size and male predominant sample. The population is select and represents individuals referred to a tertiary care center. Data is only from those CAD patients who have been chosen for angiographic evaluation or percutaneous intervention. Though cases with elevated transaminases were excluded from the study, in the absence of imaging and liver biopsy, the possibility of a concomitant Non alcoholic fatty liver disease is not excluded in our cohort. This was a cross sectional study and follow up was not available to compare outcomes in various GGT quartiles.

In conclusion, data from our study depicts association of GGT with various established risk factors in population from Northern India. Larger community based studies are needed to establish the role of GGT in development of diabetes, hypertension and metabolic syndrome in Indian population.

Conflicts of interest

None.

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