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Gamma-Glutary Transferase: A Novel Biomarker for Predicting Coronary Artery Disease

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Abstract

Background: Gamma Glutamy l Transferase (GGT) is involved in pathogenesis of various cardiovascular diseases. *Aim:* To assess serum GGT level in predicting significant CAD (Coronary Artery Disease). *Methods:* 200 patients undergoing CAG were studied. Serum GGT level was compared between normal/insignificant CAD Group (Group 1) and significant CAD Group (Group 2). Comparison between various subgroups was done. *Results:* Mean age of study population was 57.63 ± 10.78 years. Mean of serum GGT level in Group 1 was 31.61 ± 20.17 and in Group 2 was 39.48 ± 22.91. (p = 0.004). Mean ± SD of SVD, DVD and TVD were 43.29 ± 24.05, 36.8 ± 20.47 and 39.06 ± 26.04 and were not statistically significant.*Conclusion:* Serum GGT level can be used as a noninvasive biomarker to predict significant CAD.

Keywords: Gamma-glutamyltransferase; Biomarker; Coronary artery disease.

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Introduction

Coronary Artery Disease (CAD) is the major cause of morbidity and mortality worldwide. Despite extensive efforts on identification of biomarkers useful for an early assessment of CAD risk, only a few of them have been recognized. Gamma Glutamyl Transferase (GGT) is an enzyme that transfers gamma-glutamyl functional groups and responsible for the main antioxidant function. It is involved in the catabolism of glutathione, which is a major antioxidant.[1]

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Studies have showed that increased GGT level is associated with increased risk of myocardial infarction, stroke, cardiac death, atherosclerosis, arterial stiffness and plaque, metabolic syndrome and all-cause mortality.[1–3] Hence, we conducted this study to assess the correlation of serum level of GGT with severity of CAD.

Objectives of Study

1. To compare serum GGT level in patients with normal/nonobstructive CAD *versus* significant CAD;
2. To correlate serum GGT level with severity of CAD.

Materials and Methods

Source of data

Two hundred patients who had undergone coronary angiography at Sri Jayadeva Institute of

Cardiovascular Sciences and Research, Kalaguragi Branch, Karnataka from 1st March 2019 to 30th April 2019 were considered.

Methods of Collections of Data

Using a preformed proforma, data were collected for all the patients included in the study. Serum GGT level was measured in all of them. Coronary angiogram was performed to assess the severity of CAD. Correlation between serum GGT level and severity of CAD was assessed.

Inclusion criteria

All patients undergoing CAG in SJIC & R, Kalaburagi during study period.

Exclusion criteria

Those with liver disease.

Comparison was made between 2 Groups:

Group 1: Patients with normal coronaries or those with lesser than that 50% stenosis;

Group 2: Patients with significant CAD, defined as more than or equal to 50% stenosis;

p - valve of lesser than or equal to 0.05 was considered statistically significant.

Results

Mean age of the study population was 57.63 ± 10.78 years. Males were 136, females were 64. Male : Female ratio was 2.1:1. Age distribution of the study population was as depicted in, shows in (Table 1).

Diabetes Mellitus was present in 72 patients (36%). Hypertension was present in 82 patients (41%).

Severity of CAD, as found in coronary angiogram has been depicted in Table 2. Normal epicardial coronaries were seen in 12 patients, insignificant CAD was present in 10 patients, and significant CAD was seen in 178 patients. There was statistically significant difference in serum GGT level between Group 1 and Group 2. ($p = 0.004$), as shown in Table 3. Comparison between number of vessels involved and serum GGT level was done and there was significant difference between various groups. ($p = 0.007$), in Table 4. Post hac Pair wise comparisons were made between various groups and were as depicted in Table 5.

Correlation between serum GGT level and left ventricular ejection fraction was assessed and was not found to be significant. Correlation coefficient (Spearman rho) was -0.106. *p* - value was 0.133.

Table 1: Age distribution of study population

Age group	No. of Patients ($n = 200$)	Percentages
≤ 40 years	8	4
41–60 years	95	47.5
> 60 years	97	48.5

Table 2: CAG finding in study population

CAG findings	No. of patients ($n = 200$)	Percentages
SVD*	62	31
DVD*	83	41.5
TVD*	33	16.5
Insignificant CAD	10	5
Normal	12	6

*SVD - Single Vessel Disease, DVD - Double Vessel Disease, TVD - Triple Vessel Disease.

Table 3: Comparison of mean GGT between insignificant and significant CAD (2 Groups)

Groups	Nos. of Patients	Serum GGT level			Mann-Whitney *U* test
		Mean (SD)	Median (IR)	Mean rank	
Group 1	22	31.61 (20.17)	27.1 (23–29)	66.86	*p = 0.004*
Group 2	178	39.48 (22.91)	32 (26–45)	104.66	

Table 4: Comparison of mean GGT level with no of diseased vessels

Nos. of vessels involved		Serum GGT level			Kruskal-Wallis test
		Mean (SD)	Median (IR)	Mean rank	
SVD	62	43.29 (24.05)	36.25 (28.2–54)	117.06	Chi–square= 14.08 *p = 0.007*
DVD	83	36.8 (20.47)	31.7 (27–42)	101.75	
TVD	33	39.06 (26.04)	27.8 (20.4–38)	88.67	
Insignificant	10	37.08 (29.73)	23 (20.6–29.8)	72.1	
Normal	12	27.06 (1.92)	27.55 (24.75–29)	62.5	

Table 5: Post hoc pairwise comparison (Mann-Whitney *U* test)

	***p* - value**
SVD *vs* DVD	0.071
SVD *vs* TVD	0.053
SVD *vs* Insig	0.043*
SVD *vs* Normal	0.003 *
DVD *vs* TVD	0.264
DVD *vs* Insig	0.115
DVD *vs* Normal	0.006 *
TVD *vs* Insig	0.561
TVD *vs* Normal	0.048*
Insig *vs* Normal	0.456

*Suggests $p < 0.05$.

Discussion

The physiological role of GGT is to cleave the gamma-glutamyl amide bond of the tripeptide and hydrolysis of extracellular GSH to produce cysteine and other thiol ingredients. GGT is also a facilitator of the generation of Reactive Oxygen Species (ROS) and transfer gamma-glutamyl moiety of glutathione to an acceptor such as amino acid, a peptide or water.[3]

GGT is also involved in the formation and progression of atherothrombosis. It plays a role in formation of fibrous cap, plaque rupture, and erosion, increased platelet aggregation and thrombosis. There is a growing body of evidence showing the association of GGT with atherosclerosis, diabetes mellitus, hypertension and stroke.[4,5] Caliskan et al. showed that increased serum GGT level in hypertensive patients was associated with impaired coronary flow reserve.[6] Activity of GGT was also reported as an independent predictor of the thrombosis in myocardial infarction.[7] Bozbas et al. found a significant correlation between the level of GGT, CRP and metabolic syndrome.[8] Cayli et al. found that the higher serum GGT level within the "normal" range associated with a greater intima-media thickness of the thoracic aorta.[9]

Angiography is an invasive technique for the detection of CAD, but GGT can be used as a biomarker for obstructive CAD. In our study, serum GGT level was significantly different between patients with normal/insignificant CAD and significant CAD. However, it does not correlates with number of coronary arteries involved in our study.

Sheikh M studied an association of serum GGT level and premature CAD and they observed that the serum GGT level was significantly lower in normal coronary individuals. However, the post hoc pairwise comparison revealed that this difference was caused by low concentrations of GGT in normal coronary patients and patients with single double and triple vessel disease did not statistically differ regarding the GGT levels.[10] Similar results were found in our study. Mean ± SD of SVD, DVD and TVD were 43.29 ± 24.05, 36.8 ± 20.47 and 39.06 ± 26.04 and were not statistically significant. Thus, our study showed that serum GGT level can only predict presence or absence of significant CAD and not the number of vessel involved.

However, in a study by Siavash Arasteh serum GGT level predicted stenosis severity in patients with CAD. Serum GGT in patients who had ≥ 50% obstruction was higher, compared to healthy and patients with less than 50% obstruction in their coronary arteries. In this study, mean ± SD of serum GGT level in patients with SVD, DVD, TVD were 55.6 ± 9.7, 71.7 ± 12.7 and 84.7 ± 13.4 respectively, while these values in patients with normal or control group were 28 ± 10 and 17 ± 4.6, thus, suggesting progressive increase in serum GGT level with increased severity of CAD.[11]

Mao Y studied correlation between serum GGT level and CAD severity in 513 adults and found to have a positive correlation.[12]

Conclusion

Serum GGT level can be used as a noninvasive marker to predict significant CAD. However, its level may not predict the severity of CAD.

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