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Cover Page

TITLE OF MANUSCRIPT: "GAMMA GLUTAMYL TRANSFERASE LEVELS IN PATIENTS WITH ACUTE CORONARY SYNDROME: A CROSS-SECTIONAL STUDY AT A JNU IMSRC MEDICAL COLLEGE AND RESEARCH CENTER JAIPUR"

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ABSTRACT

Introduction: Oxidative stress seems to play an important role in the progression of atherosclerosis. Various researches have found Gamma glutamyl transferase (GGT) as a marker of oxidative stress and its relationship with coronary artery disease (CAD). There is lacunae in literature data exploring the changes of GGT levels in acute coronary syndrome (ACS).

Aim- To assess the prevalence of raised GGT and its correlates in ACS patients.

Methodology-Hospital based observational study conducted between April 2021 to December 2022 at Medicine department of JNU Hospital Jaipur on 155 patients of ACS .ACS was diagnosed on the basis of history, electrocardiogram and biochemical markers. The magnitude of raised GGT among ACS was 66.38% in males and 82.05% in females . The mean GGT in non ST elevated myocardial infarction (NSTEMI), ST elevated myocardial infarction (STEMI) and unstable angina (UA) was 60.60 IU/L ,55.89 IU/L and 55.77 IU/L .

Conclusion: Gamma glutamyl transferase activity is increased in subjects with ACS and elevated levels of serum GGT on admission were associated with the burden of atherosclerosis in patients with ACS.

Key words: Acute coronary syndrome, Coronary artery disease, Gamma glutamyltransferase, Oxidative stress.

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Introduction

The term acute coronary syndrome (ACS) includes unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI) and ST-segment myocardial infarction (STEMI). ACS is one of the leading causes of mortality and morbidity in the world. ACS is caused by rupture of a pre-existing atherosclerotic plaque. It is crucial to use risk stratification for managing patients with ACS which may help clinicians to identify high-risk patients who would benefit from early revascularization therapy .[1]

The main cause of arterial plaque formation, plaque rupture and clot formation during subclinical and symptomatic coronary events is inflammation.[2] The various potential inflammatory biomarkers which may have a role in early risk assessment of patients with acute coronary syndrome are CRP, interleukin 6, liver enzymes, type B natriuretic peptide and troponin, however many of them are not routinely used.[3]

Gamma-glutamyltransferase (GGT) which catalyses the first step in the degradation of extracellular glutathione (GSH), allowing for the precursor amino acids to be reused for intracellular GSH synthesis, increasing the cellular supply of GSH.GSH is crucial non-protein antioxidant of the cell and degradation of GSH can play a pro-oxidant role in various conditions; low density lipoprotein (LDL) oxidation occurs through GSH/GGT-dependent reduction and is implicated in formation of atherosclerotic plaques which may results in ACS .[4,5]

Increased serum GGT activity has been associated with worse outcomes and it predicts outcomes in patient with ischemic heart disease independent of myocardial damage, thus supplementing the prognostic information provided by traditional risk factors.[6]

Gamma glutamyl transferase is also associated with the risk factors and severity of coronary artery disease so it may help clinicians in categorizing patients into high and low risk and subsequent planning for early intervention strategy as per the risk.[7,8]

There is dearth of data linking GGT and acute coronary syndrome, therefore present study was conducted to evaluate the level of GGT in patients diagnosed with ACS and to identify the potential difference in GGT level in different types of ACS.

Aims and objectives of the study

1.To determine the frequency of raised serum Gamma Glutamyl Transferase levels in cases presenting with acute coronary syndromes.

2.To determine the association between raised GGT levels and risk factors for acute coronary syndrome.

Methodology

Hospital based observational study conducted between April 2021 to December 2022 at Medicine department of JNU Hospital Jaipur on 155 patients of ACS.

Inclusion Criteria

All patients admitted with an episode of Acute Coronary Syndrome in the Emergency care unit of SMS Hospital and willing to give consent.

Exclusion Criteria

1.History of any alcohol intake

2.History of ongoing chronic hepatobiliary disease including cirrhosis

3.Surgical conditions causing obstructive jaundice

4.History of Neoplasia

5.Enrolled in other study.

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Results

Table-1 Age group and GGT

Age Group	**Mean GGT**
<40 years	41.50
40-49 years	61.68
50-59 years	57.10
60-69 years	56.47
>=70 years	58.71

Table-2 Association of Raised GGT with various parameters

Parameters	**Total cases**	**% Of cases**	**GGT Raised cases**	**% Out of total cases**
Male	116	74.84	77	66.38
Female	39	25.16	32	82.05
DM Yes	76	49.03	60	78.95
DM No	79	50.97	49	62.03
Smoking Yes	59	38.06	50	84.75
Smoking No	96	61.94	59	61.46
HTN Present	64	41.29	49	76.56
HTN Absent	91	58.71	60	65.93
Dyslipidaemia Yes	66	42.58	46	69.70
Dyslipidaemia No	89	57.42	63	70.79
STEMI	62	40.00	38	61.29
NSTEMI	58	37.42	49	84.48
UA	35	22.58	22	62.86

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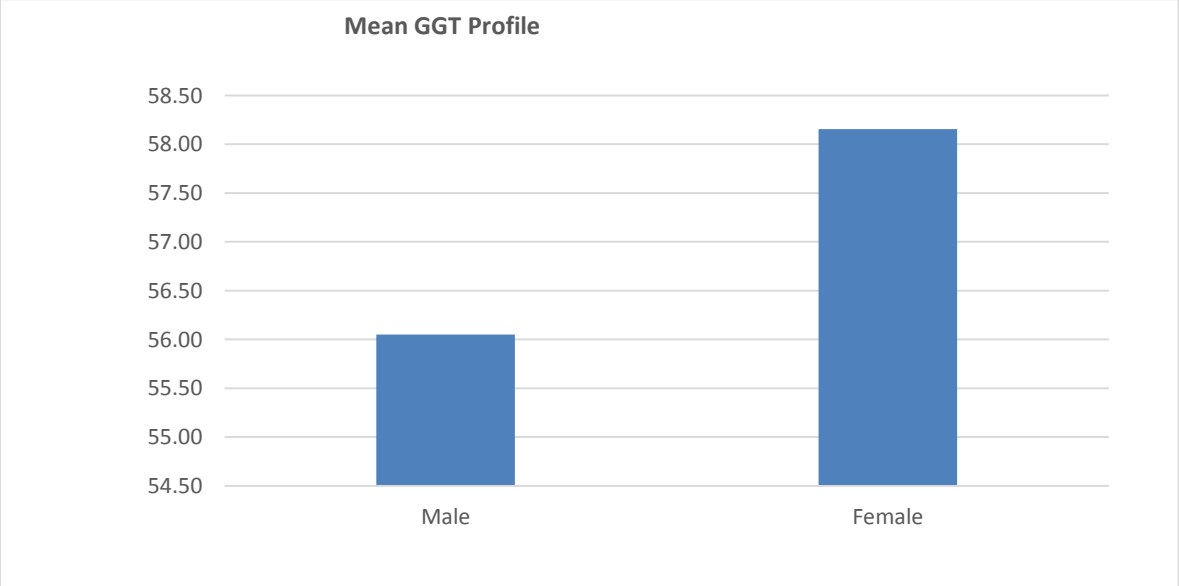
Table-3 Mean GGT in various groups

Parameter	**GGT**	
	Mean	**SD**
Male	56.05	18.20
Female	58.16	16.87
DM Yes	65.07	19.70
DM No	50.47	12.24
Smoking Yes	63.00	16.62
Smoking No	54.32	17.85
HTN Present	66.23	20.80
HTN Absent	51.57	12.34
Dyslipidaemia Yes	61.00	20.53
Dyslipidaemia No	55.12	15.20
STEMI	55.89	20.59
NSTEMI	60.60	13.51
UA	55.77	18.75



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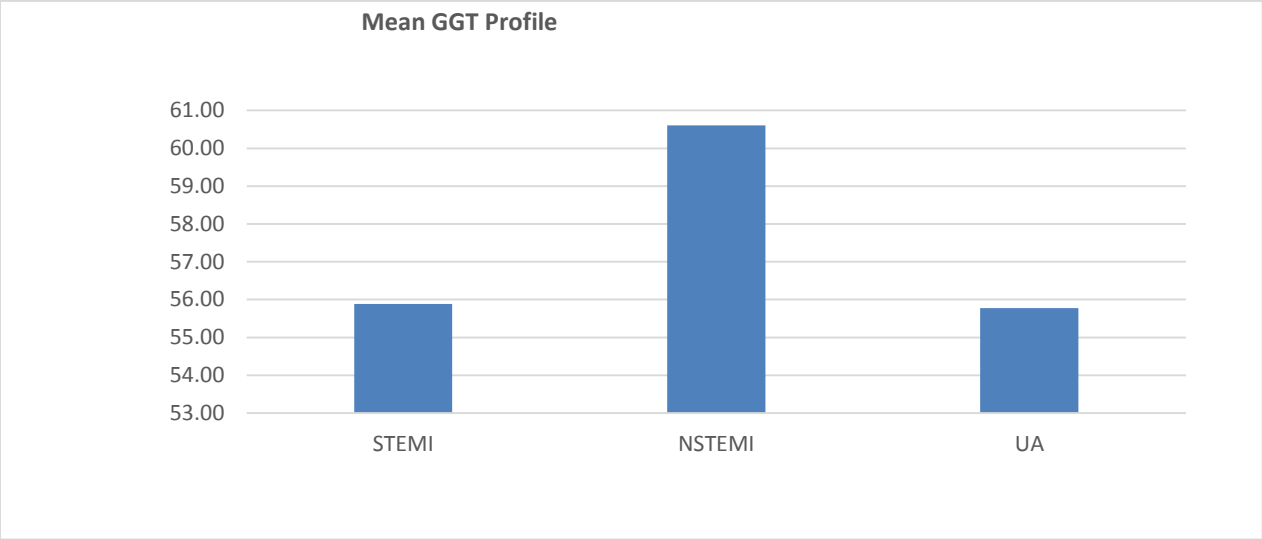

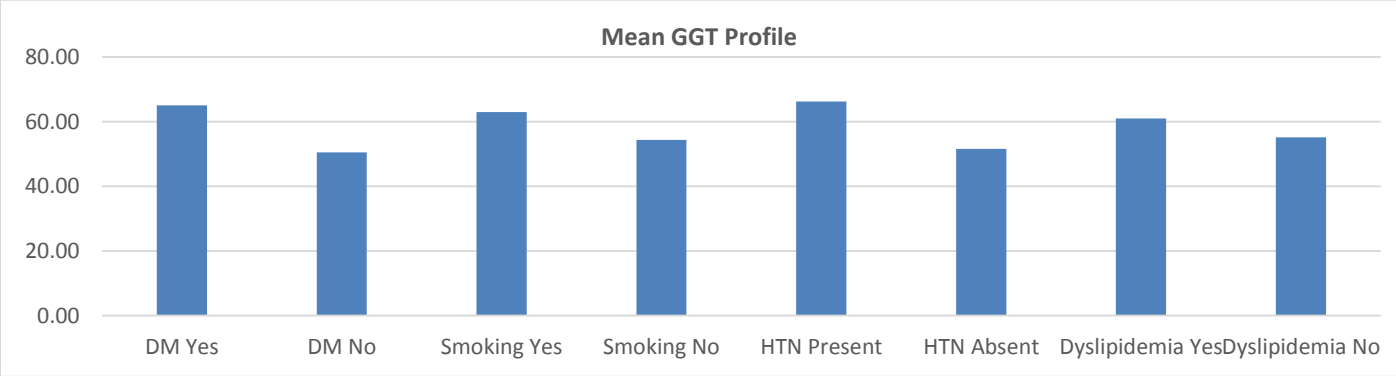

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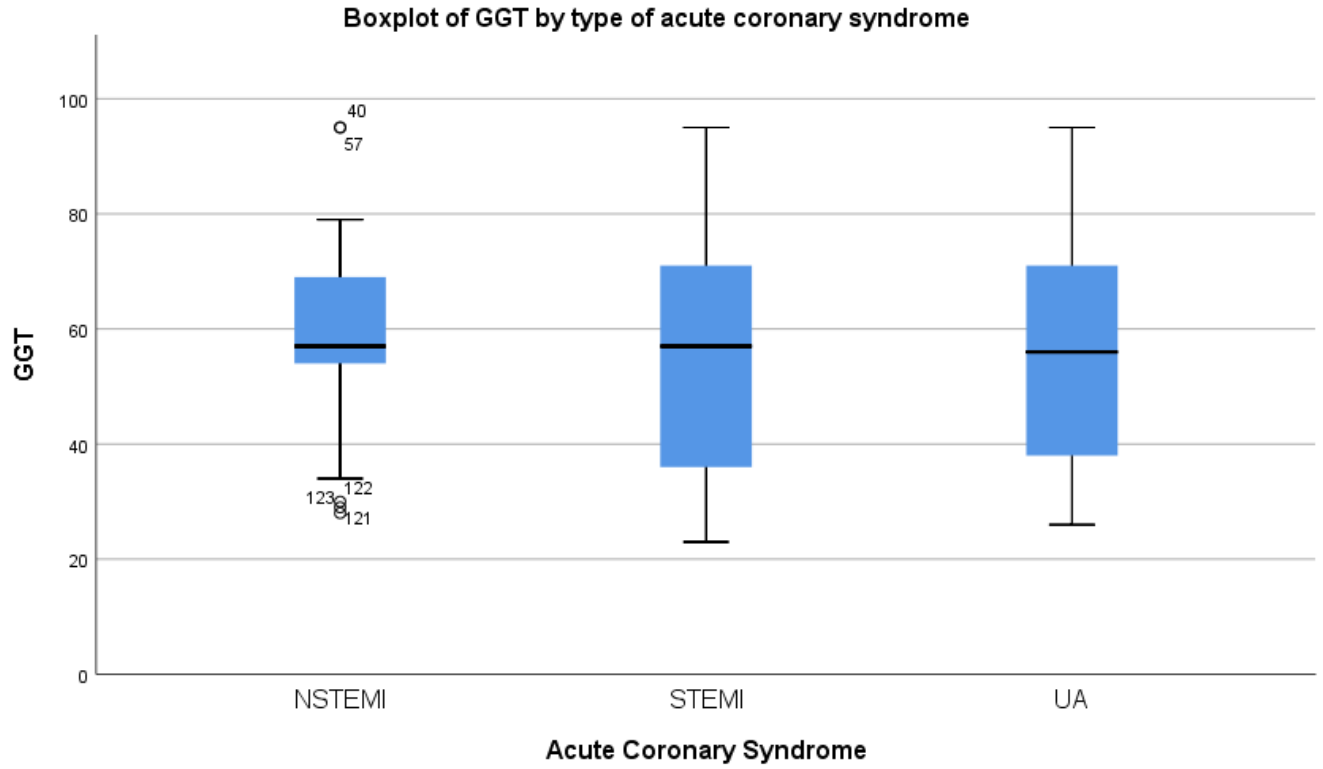

Table-4 Correlation with GGT with various parameters

Parameter	**Correlation with GGT**	
	"r"	**P value**
Gender	-0.017	0.798
DM	-0.391	<.001
Smoking	-0.237	<.001
HTN	-0.393	<.001
Dyslipidaemia	-0.147	0.029
Age	0.14	0.082
Total Cholesterol	0.1	0.215
LDL	0.171	0.034
HDL	-0.29	<.001
Vitamin B12	-0.197	0.014

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Table-5 Regression Model for GGT Raised with various parameters

	Parameters	B	Std. Error	Sig.	Exp(B)	95% Confidence Interval for Exp(B)	
						Lower Bound	Upper Bound
GGT Raised	Age	-.014	.020	.483	.986	.948	1.026
	STEMI	.157	.504	.756	1.170	.435	3.143
	NSTEMI	1.547	.550	.005	4.696	1.599	13.786
	UA	0	.	.	.	.	.
	Male	-.933	.506	.065	.393	.146	1.060
	Female	0	.	.	.	.	.
	DM Present	.645	.521	.215	1.906	.687	5.292
	DM Absent	0	.	.	.	.	.
	Smoking Yes	1.440	.501	.004	4.222	1.583	11.265
	Smoking No	0	.	.	.	.	.
	HTN Present	-.154	.574	.788	.857	.278	2.640
	HTN Absent	0	.	.	.	.	.
	Dyslipidaemia yes	-.037	.417	.929	.964	.425	2.184
	Dyslipidaemia No	0	.	.	.	.	.

Discussion- GGT and Age

In present study we found no significant association of GGT with age and gender .The mean GGT level in age group less than 40 years was 41.5 IU/L , the mean GGT level in age group 40-49 years was 61.60 IU/L , the mean GGT level in age group 50-59 years was 57.10 IU/L, the mean GGT level in age group 60-69 years was 56.47 IU/L and mean GGT level in subjects ≥70 years was 58.71 IU/L and application of t test showed that this difference was not statistically significant. Similarly Jyoti et al.[9] in their study found no significant association of age and GGT levels .However Chakraborty S et al[10] in their study found significant association of age and GGT levels

GGT and Gender

In the present study the mean GGT was higher in females than males. (58.16 IU/ml in females versus 56.05 IU/ml in males) though the difference was not statistically significant. GGT level did not show significant association with gender (p=0.798).However Jyoti et al.[9]in their study found significant association of gender and GGT levels which was inconsistent to our results (GGT more in male as compared to females).In contrast , Puukka et al[11] found statistically significant association of raised GGT with gender .They found that male patients with ACS in comparison to female patients had higher GGT levels. Possible explanation for higher values in males could be higher prevalence of risk factors like smoking and alcohol in men and seminal vesicles as an extra source of GGT production in men.

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GGT and DM

In the present study the mean GGT was higher in Diabetics than non-diabetics (65.07 IU/ml in DM patients versus 50.47 IU/ml in non-diabetics) .In present study the increased GGT level show significant association with DM ($p<0.001$). Similarly Lee DH et al.[12] in their study found that mean GGT level in DM patients was higher than non-diabetic patients which is similar to our results. Similarly Shabbir S et al.[13] in their study found that mean GGT level in DM patients was higher than non-diabetic patients which is similar to results of present study .

GGT and Smoking

In the present study the mean GGT was higher in smokers than non-smokers. (63 IU/ml in smokers versus 54.32 IU/ml in non-smokers) .In present the increased GGT level show significant association with smoking ($p<0.001$). Puukka K et al.[11] also found that GGT level show significant association with smoking which is consistent with results of present study.

GGT and Lipid profile

In the present study the mean GGT was higher in patients with abnormal lipid profile in comparison to patients with normal lipid profile.(61.00 IU/ml versus 55.12).In present study, significant association of GGT was found with dyslipidemia (association was not found with raised TG, cholesterol, LDL but show significant association with low HDL levels).However Jyoti et al.[9] in their study found no significant association of dyslipidemia and GGT levels. Shabbir S et al.[13]in their study found significant association of dyslipidemia and GGT levels which is consistent with results of present study.

GGT and ACS Category

In present study STEMI was the most common presentation of ACS (40% cases), among these patients 61.3% had raised serum GGT levels. Increase in GGT was more significant in NSTEMI than STEMI groups(60.60 IU/L in NSTEMI versus 55.8 IU/L in STEMI) and the difference between NSTEMI and STEMI on GGT level and prevalence was significant .The prevalence of raised GGT in NSTEMI was higher than STEMI (84.48% in NSTEMI versus 61.29 %in STEMI).Jyoti et al.[9] in their study found that subjects with NSTEMI had higher prevalence of raised GGT, compared to subjects with STEMI and UA which is consistent with results of present study. Similarly Emiroglu et al.[14] in their study found that GGT value varies with category of ACS and was higher in NSTEMI than STEMI which is consistent with results of present study.

Some studies had found that major adverse cardiac events (cardiovascular mortality) were independently associated with raised GGT level.14-23.However present study lacked the follow up analysis of cardiovascular event and mortality.

Conclusion

GGT activity is increased in subjects with ACS. High levels of serum GGT on admission were associated with the burden of atherosclerosis in patients with ACS. Serum GGT is a cost effective and simple vascular risk marker, its routine measurement on admission may be helpful in determining high risk patients of ACS in clinical practice. Further studies with larger numbers of patients will provide more informative data on this subject.

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