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Study on the Impact of Serum Gamma-Glutamyl Transferase (GGT) level and other Risk factors on Stroke and its Clinical Relevance.

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Abstract:
Elevated serum GGT levels have been proposed as an independent predictor for cardiovascular morbidity and mortality. The aim of this study was to evaluate the impacts of serum GGT level and other risk factors on stroke and its clinical relevance.
Total of 100 patients with stroke and 75 control were included in the study. The patients were divided into ischemic and hemorrhagic stroke according to finding from NCCT brain and/or diffusion MRI, and evaluated for serum GGT levels and presence of diabetes mellitus (DM), hypertension (HT),dyslipidemia (DL),smoking and alcohol consumption.
The frequency of DM, HT.DL and gender distributions were similar. The mean GGT levels were significantly higher in the patients as compared to control (p-0.025). Increased mean GGT levels were found in the acute ischemic patients subgroup with HDL-cholesterol (HDL-C) (p-0.031)l and VLDL-cholesterol (VLDL-C)(p-0.033). Statistically significant difference were found between embolic and lacunar infarct patients in respect to GGT level, triglyceride(TG),total cholesterol(TC),LDL-cholesterol (LDL-C) ,hypertension, diabetes and alcohol consumption (p-<0.05). When patients were compared in respect to ischemic and hemorrhagic stroke, statistically significant differences were obserbed in GGT level, hypertension and smoking (p-<0.05).
Conclusion.
Higher serum GGT levels in stroke patients reinforce the relationship with inflammation and oxidative stress. The observation of higher GGT levels in patients with relatively large areas of infarction and hemorrhagic stroke is indicative of a positive correlation between type and size of stroke and elevated serum GGT levels.

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I. Introduction:-

Gamma-Glutamyl Transferase (GGT) mediates intracellular intake of glutathione, which is an important component of antioxidant mechanism. Glutathione is produced during normal metabolic process and plays an important role in the protection of cells against oxidative stress [(1)]. GGT is used as a biomarker to determine risk for cardiovascular and cerebrovascular diseases. GGT has a prognostic role in CVD and stroke. A positive correlation has been demonstrated between higher serum GGT levels and advanced age, male gender, increases in body mass index, sedentary life style, smoking, metabolic syndrome, tachycardia, menopause and oral contraceptive use[(2)].Positive correlation between GGT level and cardiovascular mortality, namely from ischemic heart disease was found ,irrespective alcohol consumption[(22-24)]. The aim of our study was to identify the effect of serum GGT level and other risk factors in different types of strokes and its clinical relevance.

II. Material & Method:-

The patients admitted in the Department of Medicine, Rajendra Institute of Medical Sciences (RIMS), Ranchi, Jharkhand, India from 1st May, 2019 to 1st July, 2020 and diagnosed with strokes in the first 24 hours of admission were included in the study. Hundred patients with stroke and seventy five controls who had no cerebrovascular diseases were included in the study. Among 100 patients, 75 patients had ischemic stroke and 25 patients had hemorrhagic stroke.

The distinction between hemorrhagic and ischemic strokes was made according to non- contrast computed tomography (NCCT) and diffusion MRI examination. Lacunar and large infarcts were evaluated together. Patients with ischemic stroke were divided into two groups-large and embolic and lacunar and atherosclerotic infarcts. The distinction between atherosclerotic and lacunar and embolic and large was made according to the presence of atrial fibrillation (AF), characteristics of lesion in CT and diffusion MRI, the presence of thrombus in the echo-cardiography and doppler ultra- sonography, valvular heart disease and a history of the use of anticoagulants and history of the patients (recent attack of MI, the presence of cardiomyopathy, valvular heart disease, chronic sinoatrial dysfunction, inter-atrial septal anomaly). Patients with history of hypertension, diabetes, alcohol consumption and smoking were recorded.

Exclusion criteria were.(1) Giving blood after intravenous fluid replacement or treatment by any means (e.g. resuscitation) after admission, (2) Presence of known chronic liver diseases, kidney diseases or presence thyroid dysfunction (3) Presence of active infections, history of neoplasia, presence of transient ischemic attack (TIA) (4) admission to the hospital 24 hours after the first symptom (5) Absence of laboratory results, and (6) Those patients for which CT and diffusion MRI could not be performed.

The age, gender, co-morbid diseases (HT, DM, history of smoking and alcohol consumption, previous history of stroke, laboratory parameters (glucose, total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol, VLDL-cholesterol, serum GGT, SGOT,SGPT) were recorded on the study forms.

Biochemical parameters were assessed using Abott C-autoanalyser in the study.

SPSS16 statistical software was used for data analysis. Kosmogorov-Smirnov test was used for coherence of normal distribution of variables. Student t-test was used in pair wise group analysis of continuous variables which were normally distributed and data were represented as mean ± standard deviation. Mann Whitney U test was used in pair wise analysis of continuous and ordinal variables, which were not normally distributed and the data were represented as median (quarters of 25-75%), categorical data was compared using Pearson's Chi square test and was represented as numbers-percentages. P-values less than 0.05 (<0.05) were considered statistically significant.

III. Results:-

A total of 459 patients were examined and 100 eligible (according to criteria used) were included in the study. Among all participants, (25%) had hemorrhagic and (75%) had ischemic stroke. Among these, 13 (17.33%) of ischemic stroke patients had stroke in lacunar base and 62 (82.67%) had stroke in the embolic and large base (Table-1).

Table-1. . Basic demographic features of the patients with stroke and control.

Variable	Case	Control	P-value
Age (Mean±SD)	61.37±8.20	60.42±8.54	0.490
Gender	46.6-±33.7	46.6±35.8	0.743
GGT	69.6±40.0	42.8±32.1	0.025*

* Statistically Significant

Significant difference was not found between groups regarding mean ages and gender distribution. The frequencies of hypertension (56.3% versus 55.9%), diabetes mellitus (33.5% versus 34.2%), dyslipidemia (36.6% versus 38.1%), smoking (64.3% versus 66.0%) and alcohol consumption (50.2% versus 49.8%) in cases with stroke and control were comparable. Mean GGT levels in patients with stroke group was found to be statistically significantly higher (P-0.025) relative to control group.

In acute stroke cases, there was no statistical significant difference between male and female when compared with serum GGT level (Chi square value-53.879, df-52 and P-0.402).

In acute strokes cases when patients were compared in respect to gender, statistically significant difference was found in smoking as depicted in table-2,but no significant differences were found in respect to age, type of stroke, GGT level, lipid profile, hypertension , diabetes and alcohol consumption..

Table-2. Demographic and Biochemical Characteristics of acute Stroke patients in relation to Gender (Male-62,Female-38).

Characteristics	Chi square Value	Df	P- Value
Age	33.241	30	0.312
Type of Stroke (Ischemic,hemorrhagic)	1.415	1	0.234
GGT	56.919	53	0.331
Total Cholesterol	67.408	58	0.186
Triglycerides	54.372	50	0.312
HDL-Cholesterol	23.294	27	0.669
LDL-Cholesterol	58.687	48	0.139

VLDL-Cholesterol	21.085	23	0.576
Hypertension	0.321	1	0.571
Diabetes	1.073	1	0.300
Smoking	10.866	1	0.001*
Alcohol Consumption	2.554	1	0.110

* Statistically Significant

The below table-3, revealed that the serum GGT levels had statistically significant difference between ischemic and hemorrhagic stroke (P-0.045). Again statistically significant difference was found in hypertension among acute stroke cases when compared between hemorrhagic and ischemic stroke (P-0.016), but no differences were seen in respect to age, total cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol, VLDL-cholesterol, diabetes, smoking and alcohol.

Table-3. Demographic and Biochemical Characteristics of Stroke in relation to Type of Stroke.

Characteristics	Hemorrhagic(N-25) (Mean±SD)	Ischemic (N-75) (Mean±SD)	P-Value
Age	61.720±10.714	60.626±8.026	0.590
GGT	33.560±17.703	70.386±90.003	0.045*
Total Cholesterol	1.763±35.283	1.766±39.454	0.970
Triglycerides	1.275±37.376	1.380±47.643	0.308
HDL-Cholesterol	46.520±6.225	45.533±8.749	0.604
LDL-Cholesterol	1.032±29.327	1.058±27.840	0.689
VLDL-Cholesterol	23.320±5.444	24.493±9.084	0.544
Hypertension	0.840±0.374	0.573±0.497	0.016*
Diabetes	0.400±0.500	0.373±0.486	0.814
Smoking	0.840±0.374	0.786±0.412	0.588
Alcohol Consumption	0.720±0.458	0.626±0.486	0.402

* Statistically Significant

When acute ischemic patients were compared in respect to size of infarcts (embolic/large and lacunar/atherosclerotic) regarding demographic and biochemical characteristics, statistically significant differences were observed in serum GGT level (P-0.026), total cholesterol (P-0.000), triglycerides (P-0.015), LDL-cholesterol (P-0.001), hypertension (p-0.001), diabetes (P-0.016) and alcohol consumption (P-0.049), but no significant difference were seen in respect to age, HDL-cholesterol, VLDL-cholesterol and smoking as detailed in table-4.

Table-4. Demographic and Biochemical Characteristics of Size of Ischemic Stroke

Charactristics	Embolic/Large Infact Total No.62 (82.67%) Mean Rank	Lacunar/Small Infact Total No. 13(17.33%) Mean rank	P-Value
Age	37.40	40.88	0.598
GGT	40.56	25.77	0.026*
Total Cholesterol	44.08	9.00	0.000*
Triglycerides	40.81	24.62	0.015*
HDL-Cholesterol	38.07	37.65	0.950
LDL-Cholesterol	41.97	19.08	0.001*
VLDL-Cholesterol	39.96	28.65	0.088
Hypertension	41.30	22.27	0.001*
Diabetes	40.33	26.88	0.016*
Smoking	38.14	37.35	0.867
Alcohol Consumption	39.90	28.92	0.049*

* Statistically Significant (Mann Whitney U Test)

IV. Discussion:-

The serum Gamma-Glutamyl Transferase (GGT) is mostly found within cytosols as well as on cellular membrane and plays a role in intracellular ingress of amino acids and peptides in the form of gamma-glutamyl peptides. Glutathione is its most important substrate. In conditions giving rise to cellular stress intracellular glutathione levels decrease. Decreased intracellular glutathione levels induce formation of GGT enzymes so as to maintain pre-existing levels. Increased oxidative stress enhances requirement for glutathione. In the presence of inadequate amounts of glutathione, oxidative stress exerts more harmful effect [(3-5)].

The mechanism of the relationship between cardiovascular and cerebrovascular risk factors and GGT level is not fully known. The predictive role of serum GGT activity in the development of new cases of diabetes, hypertension and ischemic stroke has been established [(6-10)]. Mechanism related to oxidative stress and sub-clinical inflammation can account for the role of GGT in the development of cerebrovascular disease [(13-16)].

Increased serum GGT levels can play a pathogenetic role in the evolution and instability of atherosclerotic plaques in different vascular region [(17)]. Serum GGT is a well assessed marker of alcohol abuse, higher serum GGT levels are also found to be independently correlated with conditions associated with increased atherosclerosis such as obesity, elevated serum cholesterol, high blood pressure, alcohol consumption and myocardial infarction [(18-21)].

In one study[(11)], an independent but significant association between serum GGT levels and cardiovascular mortality was found, a significant correlation between serum GGT and cardiovascular disease was also found but a statistically significant correlation between GGT levels and stroke (both ischemic and hemorrhagic types) could not be detected. Besides, prognostic significance of serum GGT was more prominently observed in patients younger than 60 years of age. In our study, GGT levels were statistically significantly higher in the stroke group related to control group.

In another study [(12)], it was found that serum GGT is a sensitive early stage predictor of oxidative stress as a risk factor for the development of diabetes and hypertension. In our study, statistically significant difference was observed in ischemic stroke patients with or without hypertension and diabetes and also in patients with ischemic and hemorrhagic stroke with or without hypertension.

In our study, significantly high GGT levels were detected in the acute stroke group relative to the control group. Besides, statistically significantly higher levels of GGT in cases with dyslipidemia, hypertension, diabetes, smoking and alcohol consumption suggest the role of oxidative stress. The serum GGT might increase secondary to arterial wall inflammation and resultant arterial wall thickening.

V. Conclusion:-

Higher GGT levels in acute stroke patients relative to the control group reinforce the relationship of GGT with inflammation and oxidative stress. Detection of relatively higher levels of GGT in acute stroke patients with hypertension, dyslipidemia and diabetes indicates the presence of a positive correlation between GGT levels, oxidative stress and inflammation, when compared with embolic and atherosclerotic group of patients, Observation of higher GGT levels in embolic and hemorrhagic stroke is indicative of a positive correlation between increases in infarcts size, type of stroke and elevated GGT levels.

VI. Recommendation:-

From the present study, it was revealed that significantly higher serum GGT levels were present in cases of hemorrhagic stroke and large ischemic stroke as compared to control. Therefore, the elevated level of serum GGT can be considered as an independent risk factor for the various types and severity of stroke.

The clinicians who deals with the cases of stroke, will have to keep themselves on alert that elevated serum GGT levels along with other associated risk factors may have influence on type and severity of strokes and accordingly therapeutic intervention be planned to improve prognosis and to reduce morbidity and mortality of stroke patients and.

Further studies with large sample size will be required for better validation and possible role of serum GGT in the prediction of oxidative stress and degree of inflammation.

References:-

[1]. Nurbanu Gurbuzer, Eren Gozke, and Zeliha Ayhan Basturk, Gamma-Glutamyl Transferase Levels in Patients with Acute Ischemic Stroke, Cardiovasc Psychiatry Neurol. 2014; 2014: 170626. Published online 2014 Aug 18.

[2]. Kim DJ, Noh JJ, Cho NH, et al. Serum γ-glutamyl transferase within its normal concentration range is related to the presence of diabetes and cardiovascular risk factors. Diabetic Medicine. 2005;22(9):1134–1140.

[3]. Shimizu Y, Imano H, Ohira T, et al. γ-glutamyl transpeptidase and incident stroke among japanese men and women: the circulatory risk in communities study (CIRCS) Stroke. 2010;41(2):385–388.

[4]. Lee D, Blomhoff R, Jacobs DR, Jr. Is serum gamma glutamyl transferase a marker of oxidative stress? Free Radical Research. 2004;38(6):535–539.

[5]. Paolicchi A, Minotti G, Tonarelli P, et al. γ-Glutamyl transpeptidase-dependent iron reduction and LDL oxidation: a potential mechanism in atherosclerosis. Journal of Investigative Medicine. 1999;47(3):151–160.

[6]. Yamada J, Tomiyama H, Yambe M, et al. Elevated serum levels of alanine aminotransferase and gamma glutamyltransferase are markers of inflammation and oxidative stress independent of the metabolic syndrome. Atherosclerosis. 2006;189(1):198–205.

[7]. Ikai E, Honda R, Yamada Y. Serum gamma-glutamyl transpeptidase level and blood pressure in nondrinkers: A possible pathogenetic role of fatty liver in obesity-related hypertension. Journal of Human Hypertension. 1994;8(2):95–100.

[8]. Yamada Y, Ikai E, Tsuritani I, Ishizaki M, Honda R, Ishida M. The relationship between serum γ-glutamyl transpeptidase levels and hypertension: common in drinkers and nondrinkers. Hypertension Research. 1995;18(4):295–301.

[9]. Jousilathi P, Vartiainen E, Alho H, Poikolainen K, Sillanaukee P. Opposite association of carbohydrate deficient transferrin and gama-glutamyltransferase with prevalent coronary heart disease. Archives of Internal Medicine. 2002;162(7):295–301.

[10]. Perry IJ, Wannamethee SG, Shaper AG. Prospective study of serum γ-glutamyltransferase and risk of NIDDM. Diabetes Care. 1998;21(5):732–737.

[11]. Nakanishi N, Nishina K, Li W, Sato M, Suzuki K, Tatara K. Serum γ-glutamyltransferase and development of impaired fasting glucose or type 2 diabetes in middle-aged Japanese men. Journal of Internal Medicine. 2003;254(3):287–295.

[12]. Ruttmann E, Brant LJ, Concin H, Diem G, Rapp K, Ulmer H. γ-glutamyltransferase as a risk factor for cardiovascular disease mortality: An epidemiological investigation in a cohort of 163 944 Austrian adults. Circulation. 2005;112(14):2130–2137.

[13]. Lee DH, Jacobs DR, Gross M, et al. γ-Glutamyltransferase is a predictor of incident diabetes and hypertension: the coronary artery risk development in young adults (CARDIA) study. Clinical Chemistry. 2003; 49(8):1358–1366.
[14]. Lee DH, Ha MH, Kim JH, et al. Gamma-glutamyltransferase and diabetes—a 4 year follow-up study. Diabetologia. 2003; 46(3):359–364.
[15]. Emdin M, Pompella A, Paolicchi A. Gamma-glutamyltransferase, atherosclerosis, and cardiovascular disease: triggering oxidative stress within the plaque. Circulation. 2005;112(14):2078–2080.
[16]. Brenner H, Rothenbacher D, Arndt V, Schuberth S, Fraisse E, Fliedner TM. Distribution, determinants, and prognostic value of γ-glutamyltransferase for all-cause mortality in a cohort of construction workers from Southern Germany. Preventive Medicine. 1997;26(3):305–310.
[17]. Pompella A, Emdin M, Passino C, Paolicchi A. The significance of serum gamma-glutamyltransferase in cardiovascular diseases. Clinical Chemistry and Laboratory Medicine. 2004;42(10):1085–1091.
[18]. Emdin M, Passino C, Donato L, Paolicchi A, Pompella A. Serum γ-glutamyltransferase as a risk factor of ischemic stroke might be independent of alcohol consumption. Stroke. 2002;33(4):1163–1164.
[19]. Nilssen O, Førde OH, Brenn T. The Tromsø Study: distribution and population determinants of gamma-glutamyltransferase. Am J Epidemiol. 1990; 132: 318–326.
[20]. Daeppen JB, Smith TL, Schuckit MA. Influence of age and body mass index on γ-glutamyltransferase activity: a 15-year follow-up evaluation in a community sample. Alcohol Clin Exp Res. 1998; 22: 941–944.
[21]. Betro MG, Oon RC, Edwards JB. Gamma-glutamyl transpeptidase and other liver function tests in myocardial infarction and heart failure. Am J Clin Pathol. 1973; 60: 679–683.
[22]. Wannamethee G, Ebrahim S, Shaper AG. Gamma-glutamyltransferase: determinants and association with mortality from ischemic heart disease and all causes. Am J Epidemiol. 1995; 142: 699–708.
[23]. Brenner H, Rothenbacher D, Arndt V, Schuberth S, Fraisse E, Fliedner TM. Distribution, determinants, and prognostic value of gamma-glutamyltranspeptidase for all-cause mortality in a cohort of construction workers from south Germany. Prev Med. 1997; 26: 305–310.
[24]. Emdin M, Passino C, Michelassi C, Titta F, L'Abbate A, Donato L, Pompella A, Paolicchi A. Prognostic value of serum gamma-glutamyl transferase activity in patients with ischaemic heart disease. Eur Heart J. 2001; 22: 1802–1807.

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