ORIGINAL ARTICLE

Association between Ischemic Stroke and Raised Serum Gamma-Glutamyl Transferase

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ABSTRACT

Background: Prevalence of Ischemic stroke is on rise. New and novel indicators of disease severity and outcome like raised serum Gamma-glutamyl transferase may help us reduce the morbidity.
Objective: To determine the association between ischemic stroke and raised serum Gamma-glutamyl transferase.
Methods: This case-control study was carried out at Medical Emergency Department, Lahore General Hospital, Lahore in six months from 24th February to 23rd August 2015. One hundred and ninety five cases (patients with first-ever episode of acute ischemic stroke) presenting within 24 hours were included. Included One hundred and ninety five controls were healthy attendants of patients matched by age (within 5 years) and gender but without history of cardiovascular diseases i.e. ischemic heart disease, ischemic stroke and peripheral vascular disease. Frequency of raised gamma-glutamyl transferase was determined among cases and controls.
Results: Out of 390 patients 88 (22.6%) had raised GGT. 26.7% of cases and 18.5% among controls had raised gamma-glutamyl transferase (p value > 0.05). Odds ratio came out 1.44 ((at 95% CI, 0.992 to 2.103). There was no effect of age, gender, smoking, BMI on the outcome.
Conclusion: There is no association between raised gamma-glutamyl transferase and ischemic stroke as the frequencies of raised gamma-glutamyl transferase were comparable among cases and controls.
Keywords: Raised gamma-glutamyl transferase, Ischemic stroke, Gamma-glutamyl transferase

INTRODUCTION

Stroke entails a high socioeconomic burden due to increased morbidity and mortality and more commonly affects elderly patients who comprise a continuously increasing proportion of the population in developed countries[1,2]. Ischemic stroke accounts for more than 80% of total stroke events[3-5]. Early identification of individuals at risk may be helpful in designing primary prevention strategies. The identification of risk predictors may help clinicians to triage patients at greater risk[6,7]. Serum gamma-glutamyl transferase (GGT) has been conventionally considered a marker of excessive alcohol intake and/or liver dysfunction. There is accumulating evidence suggesting a prognostic role of GGT in cardiovascular diseases (CVD) including stroke[1,2,8].

Recent data indicate an active involvement of gamma-glutamyl transferase in the pathogenesis of atherosclerosis through oxidative and inflammatory mechanisms. GGT activity favours the cellular supply of GSH, the most important non-protein antioxidant of the cell and thus it counters ooxidative stress[9]. It makes GGT a potentially valuable addition to the growing list of clinically available tests useful in initially stratifying patient risk. In a study, percentage of stroke patients presenting with high [>27 IU/L) GGT levels was greater than controls (28.8% vs. 16.9%). Compared to subjects with GGT levels in the lowest quartile, those within the highest quartile had a 4.7-times increase in the odds of experiencing an ischemic stroke (95% CI 2.39-9.11, p< 0.001). This association remained significant after controlling for all potential confounders (adjusted OR, 2.90, 95% CI, 1.35-6.27; p <0.007).[3]

SUBJECTS AND METHODS

This case-control study was carried out at Medical Emergency Department, Lahore General Hospital, Lahore in six months from 24th February to 23rd August 2015. Patients age between 40-80 years, either sex, patients with first-ever episode of acute ischemic stroke presenting within 24 hours and healthy attendants of patients matched by age (within ±5 years) and gender but without history of cardiovascular diseases i.e. ischemic heart disease, ischemic stroke and peripheral vascular disease were included. Any liver disease determined by abnormal ALT and ultrasonography (coarse echo texture, hepatomegaly or fatty infiltration), history of alcohol

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intake, chronic kidney disease (creatinine >1.4 mg/dl) and history of previous stroke were excluded. One hundred and ninety five consecutive cases with ischemic stroke were included and also 195 controls were enrolled preferably the accompanying healthy attendants of the patients. CT scan of brain was performed and diagnosis was confirmed. Under aseptic conditions, venous blood samples were obtained from cases at the time of presentation in emergency department for baseline laboratory examination. Serum Gamma-glutamyl transferase was measured by using standard chemical analyzer. Data was collected in a structured proforma containing background information like age, sex and raised GGT. HbA1c >7%, history of current smoking and presence of dyslipidemia were recorded additionally to cater for effect modification. Data was analyzed using SPSS version 21. Association was determined by measuring odds ratio in both groups. Data was stratified for effect modifiers using chi square test. A p value ≤05 was taken as significant.

RESULTS

In our study population 390 patients were included with mean age of 53.68±9.47 ranged from 40 to 70 years. Two hundred and seventy seven patients (58.2%) in our study population were less than 55years of age whereas 163 patients (41.8%) were either 55 years or more in age. Two hundred and eighty eight patients (73.8%) among our sampled population were male and remaining 102 patients (26.2%) were female. Out of 390 patients 88(22.6%) had raised GGT. HbA1c level in 62 patients (15.9%) were above 7% while in rest of 328 patients (84.1%) it was below or equal to 7%. 27 patients (6.9%) were currently smoking while rest of 363(93.1%) were non-smoker. Only 59 patients (15.1%) were having dyslipidemia (Table 1). When we cross tabulated our study group (case & control) with raised GGT and applied Pearson chi square test, the results came out n0n-significant (p=0.053). Raised GGT was statistically equally distributed among cases and controls [26.7% vs 18.5%] (Table 2). When the data was stratified the cross tabulated group and raised GT with gender, among male patients of cases and control group with raised GGT level showed up non-significant results (p=0.130), similarly non-significant results were seen in cases and controls of female patients [p=0.246] (Table 3). When we stratified the cross tabulated group and raised GGT with age group, in cases and control group of patients with age below 55 years showed up non-significant results (p=0.155), similar results were seen in cases and controls of age group above 55 years [p=0.053] (Table 4). When we stratified the cross tabulated group and raised GT with HbA1c > 7% , patients of cases and control group with raised GGT level showed up non-significant results (p=0.644) among patients with HbA1c > 7% of sampled population (Table 5). When we stratified the cross tabulated group and raised GT with dyslipidemia patients, cases and control group with raised GGT level in dyslipidemia patients showed that, there was not a single patients of dyslipidemia with no raised GGT (Table 6).

Table I: Demographic information of the patients

Variable	No.	%
Gender		
Male	288	73.8
Female	102	26.2
Age (years)		
< 55	227	58.2
> 55	163	41.8
Raised GGT		
Yes	88	22.6
No	302	77.4
HbAlc >7%		
Yes	62	15.9
No	328	54.1
Current smokers		
Yes	27	6.9
No	363	93.1
Dyslipidemia		
Yes	59	15.1
No	331	84.9

Table 2: Comparison of case and control groups with raised GGT

Group	Raised GGT	
	Yes (%)	No (%)
Case	52 (25.7%)	143 (73.7%)
Control	36 (18.5%)	159 (81.5%)

Odds ratio= 0.623, at 95% CI, (.385 to 1.007) P>0.053 (NS)

Table 3: Comparison of groups in genders according to raised GGT

Gender	Raised GGT		P value
	Yes	No	
Male			
Case	38	109	0.130 (NS)
Control	26	115	
Female			
Case	14	34	0.246 (NS)
Control	10	44	

Table 4: Comparison of groups in age according to raised GGT

Age (years)	Raised GGT		P value
	Yes	No	
< 55			
Case	27	85	0.155 (NS)
Control	19	96	
> 55			
Case	17	58	0.053 (NS)
Control	42	63	

Table 5: Comparison of groups in HbAIc >7% according to raised GGT

HbAIc >7%	Raised GGT		P value
	Yes	No	
Yes			
Case	6	31	0.728 (NS)
Control	3	22	
No			
Case	46	112	0.040 (S)
Control	33	137	

Table 6: Comparison of groups in dyslipidemia according to raised GGT

Dyslipidemia	Raised GGT		P value
	Yes	No	
Yes			
Case	23	-	
Control	36	-	
No			
Case	29	143	0.000 (S)
Control	-	159	

DISCUSSION

Ischemic stroke accounts for more than 80% of total stroke events. Early identification of individuals at risk may be helpful in designing primary prevention strategies. Mortality secondary to complications of ischemic stroke can be reduced if patients are stratified early. Gamma-glutamyl transferase is widely available chemical pathology test and routinely used as a marker of liver pathology.[9.10] In our study, 26.7% of cases and 18.5% of controls has raised gamma-glutamyl transferase. This result implies a higher frequency of raised gamma-glutamyl transferase in patients with first episode of ischemic stroke. These results are comparable with previous studies.[11,12] In a study, percentage of stroke patients presenting with high [>27 IU/L) GGT levels was greater than controls (28.8% vs. 16.9%).

But contrary to previous studies, the difference was statistically non-significant (p value > 0.05).[12,13] Odds ratio ranged from 0.992 to 2.103 (at 95% CI) and came out 1.44. It implies that raised GGT was equally distributed among cases and controls. In the previous study, compared to subjects with GGT levels in the lowest quartile, those within the highest quartile had a 4.7-times increase in the odds of experiencing an ischemic stroke (95% CI 2.39-9.11, p< 0.001).[13] This association remained significant after controlling for all potential confounders (adjusted OR, 2.90, 95% CI, 1.35-6.27; p <0.007). [7] The difference may be secondary to sample size, sampling technique and socio demographic difference.

CONCLUSION

It is concluded that at current sample size, we accept the null hypothesis that there is no association between raised gamma-glutamyl transferase and ischemic stroke as the frequencies of raised gamma-glutamyl transferase were comparable among cases and controls.

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