Research Letter

Association Between Serum Gamma-glutamyl Transferase Level and Hypertension in Indian Adults: A Population Based Cross-Sectional Study

Gamma Glutamyl Transferase (GGT) is an enzyme responsible for initiating extracellular catabolism of glutathione in mammalian cells.[1] Recent studies suggest a possible role of GGT in the pathogenesis of hypertension. A literature search was carried out to identify studies conducted with the objective of finding association between hypertension and GGT. It revealed that there is dearth of studies conducted with similar objective.[2-6] The present study was conducted in this backdrop to explore any possible association between hypertension and GGT in Indian population. In our study, 194 patients consented of which 96 patients were hypertensive and 98 normotensive. The age and sex of participants in either group did not show any statistical difference. The systolic blood pressure (expressed as Mean ± Standard deviation in mm of Hg) in normotensive and hypertensive group was 116 ± 8.2 and 148 ± 6.8, respectively, while the diastolic blood pressure (in mm of Hg) in normotensive and hypertensive group was found to be 76 ± 3.2 and 96 ± 4.8, respectively. The GGT level was (38.98 ± 7.53) IU/L in the normotensive arm as compared with (42.23 ± 9.06) IU/L in the hypertensive arm ($P < 0.001$). The present study indicates that GGT level is elevated in hypertensive patients as compared with their age and sex matched normotensive peers suggesting a positive association between the two.

A population-based cross-sectional study was conducted to address the study objective. The study was approved by the institutional ethics committee. All consecutive patients attending the biochemistry laboratory of the institute were considered eligible for participation using the following inclusion–exclusion criteria.

Patients of either sex with age between 15 and 65 years. Patients were excluded if there is history or clinical evidence of (1) Diabetes Mellitus, (2) Renal Disease, (3) Liver Disease, (4) Cardiac Disease, (5) Active Infection, or (6) Acute Illness.

On the first day (Study day 0), each patient was explained about the details of the study rationale and confidentiality safeguards. Only those patients who gave their written consent were included in the study. Following informed consent administration, blood pressure (BP) was measured by a physician of the trial team. The BP measurement was repeated for next two consecutive days (Day 1, 2). Patients who were found to have Systolic Blood Pressure (SBP) higher than 140 mmHg and/or Diastolic Blood Pressure (DBP) higher than 90 mmHg on three consecutive days were considered as hypertensive. On the Study day 2, blood sample were collected from all the study participants for estimation of serum GGT. All samples were immediately centrifuged and stored at 2–8°C until analysis for the relevant biochemical parameters. All analyses were performed within 3 hours of sample collection. Serum GGT level was measured by XL600 (Transasia Bio- mediclas Limited)autoanalyzer using Gamma Glutamyl p-Nitroanilidine (GPNA) principle.[7]

The statistical software R version 2.11.1 was used to analyze the data. All values were expressed as mean + standard deviation unless otherwise indicated, and differences in mean values between two groups were analyzed using Student's *t*-test. All tests were two tailed and considered statistically significant if $P <$ level of significance, 0.05.

A total of 194 patients consented into the study of which 96 patients were hypertensive and 98 normotensive. In the present study, the age of the patients in hypertensive group was 56.71 ± 8.48 years as compared with 57.72 ± 11.28 years in the normotensive group ($P = 0.47$).The male:female ratio between the two groups did not show any significant statistical difference ($P < 0.99$). However, the Body Mass Index (BMI) of the hypertensive group was 32 + 4.1 as compared with 27 + 2.3 in the normotensive group ($P < 0.0001$). The SBP in normotensive and hypertensive group was 116 ± 8.2 and 148 ± 6.8, respectively, while the DBP in normotensive and hypertensive group was found to be 76 ± 3.2 and 96 ± 4.8, respectively. The GGT level was (38.98 ± 7.53) IU/L in the normotensive arm as compared with (42.23 ± 9.06) IU/L in the hypertensive arm ($P < 0.001$). The details are shown in Table 1.

In the present study, the age of the patients in hypertensive group was 56.71 ± 8.48 years as compared with 57.72 ± 11.28 years in the normotensive group.($P = 0.47$). The

Table 1: Baseline demographic and anthropometric data of study participants

	Normotensive group	Hypertensive group	*P* value*
Number of patients	98	96	
Male/Female	56/42	54/41	0.99
Age (years)	57.72+11.28	56.71+8.48	0.47
BMI	27+2.3	32+4.1	<0.0001
Systolic blood pressure (in mm of Hg)	116±8.2	148±6.8	
Diastolic blood pressure (in mm of Hg)	76±3.2	96±4.8	
Gamma glutamyltransferase (U/L)	38.98±7.53	42.23±9.06	<0.001

*A two-tailed *P*-value <0.05 is considered to be statistically significant

male:female ratio between the two groups did not show any significant statistical difference (*P* value 0.99). Thus, the present study suggests that serum GGT levels are elevated in hypertensive patients as compared with their age and sex matched normotensive peers ($P < 0.001$). Our results are in agreement with previous studies that reported a positive association between higher serum GGT level and clinical hypertension.[2-6] Our results are also in concordance with the current understanding of the role of GGT in hypertension development. A mechanism has been put forward to account for the pathological role of GGT in elevation of BP. GGT is known to act as an antioxidant by virtue of its central role in GSH cycle. Hypertension being a state of high oxidative stress elevated GGT level can be explained as a compensatory mechanism.[8] Furthermore, recent studies have revealed a pro-oxidant generating role of GGT. GGT generates Reactive Oxygen Species (ROS) in presence of free iron or other transition metal. These authors suggested that the GGT mediated generation of the more reactive thiol cysteinyl glycine could cause the reduction of ferric iron Fe(III) to ferrous Fe(II), thus starting a redox cycling process liable to result in the production of reonducted in Pakistan byactive oxygen species (ROS).[9]

Another notable finding in our study is BMI of the hypertensive group (32 + 4.1) is statistically higher than normotensive group (27 + 2.3) ($P < 0.0001$). Our finding is in congruence with the study conducted by Iqbal *et al*.[6]. Raised BMI is a measure of obesity which has many adverse effects on hemodynamics and cardiovascular function. It increases total blood volume and cardiac output thus increasing the cardiac workload. Typically, obese patients have a higher cardiac output but a lower level of total peripheral resistance at any given level of arterial pressure. Most of the increase in cardiac output with obesity is caused by stroke volume, although because of increased sympathetic activation, heart rate is typically mildly increased as well.The Frank–Starling curve is often shifted to the left because of increases in filling pressure and volume, thus increasing cardiovascular work. Obese patients are more likely to be hypertensive than lean patients, and weight gain is typically associated with increases in arterial pressure.[10,11] The study included a sample size of 194 patients attending biochemistry department of a single medical college. Adequately powered multicentric studies involving more study participants are needed to confirm the association between GGT and hypertension.

The present study indicates that GGT level is elevated in hypertensive patients compared with their normotensive peers suggesting a positive association between the two. However, adequately powered multicentric studies are needed to substantiate the association between serum GGT level and hypertension.

Subhasish Dan, Indranil Banerjee[1], Himangshu Roy[2], Shiuli Roy, Tamoghna Jana[3], Satrajit Dan[4]

Department of Biochemistry, Medical College, Kolkata, [1]Department of Clinical and Experimental Pharmacology, Calcutta School of Tropical Medicine, [2]Department of General Surgery, Medical College, Kolkata, [3]Medical Officer, Department of Medicine, Rural Hospital, Kotulpur, Bankura Satrajit Dan, [4]Medical Officer, Department of Medicine Block Primary Health Centre, Madhabdihi, Burdwan, E-mail: dronineo@yahoo.co.in

References

1. Whitfield JB. Gamma glutamyl transferase. Crit Rev Clin Lab Sci 2001;38:263-355.
2. Kotani K, Shimohiro H, Adachi S, Sakane N.The association between an increased level of gamma Glutamyl transferase and systolic blood pressure in diabetic subjects. Tohoku J Exp Med 2008;214:321-5.
3. Shankar A, Li J.Association Between Serum Gamma-Glutamyl transferase Level and Prehypertension Among US Adults. Circ J 2007;71:1567-72.
4. Lee DS, Evans JC, Robins SJ, Wilson PW, Albano I, Fox CS, *et al*. Gamma Glutamyl transferase and metabolic syndrome, cardiovascular disease, and mortality risk: The Framingham Heart Study. Arterioscler Thromb Vasc Biol 2007;27:127-133.
5. Lee DH, Jacobs DR Jr, Gross M, Kiefe CI, Roseman J, Lewis CE, *et al*. Gamma Glutamyl transferase is a predictor of incident diabetes and hypertension: The Coronary Artery Risk Development in Young Adults (CARDIA) Study. Clin Chem

2003; 49:1358-66.
6. Iqbal A, Khoja A, Iftikhar U, Mehjabeen. A comparison of the effects of Gamma Glutamyltransferase on age and obesity among normal, hypertensive and type 2 diabetics. Biomedica 2009;25:123-7. (Accessed April 24, 2011, at http://www.thebiomedicapk.com/articles/169.pdf).
7. Gamma-Glutamyl Transferse (GGT) in Refrigerated Serum–NHANES 2001-2002 Collaborative Laboratory Services, L.L.C. (Accessed November 16, 2011, at http://www.cdc.gov/nchs/data/nhanes/nhanes_01_02/l40_b_met_gamma_glutanyl_transferase_sum.pdf).
8. Ceriello A, Motz E. Is oxidative stress the pathogenic mechanism underlying insulin resistance, diabetes, and cardiovascular disease? The common soil hypothesis revisited. Arterioscler Thromb Vasc Biol 2004;24:816-23.
9. Drozdz R, Parmentier C, Hachad H, Leroy P, Siest G, Wellman M. Gamma-glutamyltransferase dependent generation of reactive oxygen species from a glutathione/transferrin system. Free Radic Biol Med 1998;25:786-92.
10. Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor of cardiovascular disease: A 26-year follow-up of participants in the Framingham Heart Study. Circulation 1983;67:968-77.
11. Lavie CJ, Milani RV, Ventura HO. Obesity and cardiovascular disease: Risk factor, paradox, and impact of weight loss. J Am Coll Cardiol 2009;53:1925-32.

Access this article online

Quick Response Code:

Website: www.najms.org

DOI: 10.4103/1947-2714.102000