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**Original Research Article**

# Utility of serum gamma glutamyl transferase activity among hypertensive patients

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## ABSTRACT

**Background:** Hypertension, a chronic medical condition of elevated blood pressure in the arteries. It is an emerging problem worldwide and one of the identifiable cause of kidney disease. Gamma glutamyl transferase (GGT) plays essential role in the metabolism of glutathione which is reported as major antioxidant. More recently increased GGT is associated with pathogenesis of hypertension. This study was aimed to determine activity of gamma glutamyl transferase in hypertensive patients.
**Methods:** All together 150 participants were recruited from Department of Medicine, Star Hospital for this hospital based cross-sectional study. Among which 50 were normotensive, 50 were pre-hypertensive and 50 were hypertensive. Blood sample were collected and analyzed in autoanalyser by enzymatic method.
**Results:** Mean serum gamma glutamyl transferase activity is significantly different among normotensive, prehypertensive and hypertensive groups (i.e., 10.3 IU/l, 26.8IU/l and 37.2 IU/l respectively). Serum gamma glutamyl transferase activity is significantly higher in prehypertensive patients than normotensive group (p=0.001). Similarly GGT activity is significantly increased in hypertensive patients than prehypertensive patients (p=0.001).
**Conclusions:** Serum gamma glutamyl transferase activity is raised in prehypertensive and hypertensive participants as compared to normotensive. Thus Serum gamma glutamyl transferase level can have potential role on management of hypertension.

**Keywords:** Hypertension, Gamma glutamyl transferase, Kidney disease

## INTRODUCTION

Hypertension also known as high blood pressure is a long term medical condition in which the blood pressure in the arteries is persistently elevated. It is an emerging problem worldwide and one of the identifiable marker of kidney disease.[1] Glutathione (glutamyl-cysteinyl-glycine) is the main antioxidant in mammalian cells and is a ubiquitous thiol-containing tripeptide, which plays a central role in cellular biology.[2]

Gamma-glutamyl transferase (GGT) is an enzyme present in serum and most cell surfaces. GGT is concentrated in the liver, but it's also present in the gallbladder, spleen, pancreas, and kidneys. It is involved in glutathione metabolism by transferring the gamma glutamyl functional group to a variety of acceptor molecules that may be amino acids, peptide or water. This reaction produces cysteinyl-glycine moieties, which are usually taken within the intracellular compartment by the action of membrane dipeptidases as precursors for glutathione resynthesis.[3] GGT is also considered as an oxidative stress marker. The reason behind this association can be

explained as; increased transport of glutathione into cells by increased GGT activity is to maintain higher level of antioxidant inside the cell to compensate the oxidative stress.[4]

Serum GGT, an enzyme that is routinely used as a diagnostic marker of liver disease, alcoholism but recently increased serum GGT levels are implicated in increased blood pressure and the progression of hypertension. More recently GGT may have a role in the pathogenesis of cardiovascular disease, diabetes mellitus, and metabolic syndrome.[5]

So this study was aimed to determine and compare serum GGT activity among normotensive and hypertensive participants.

## METHODS

This cross-sectional study was performed at the Department of Biochemsitry in collaboration with Department of medicine, Star Hospital, Lalitpur, Nepal from July 2018 to August 2019. The participants enrolled in the study were selected from among the patients attending OPD of medicine. Total of 150 participants were enrolled in study among which 50 (normotensive), 50 (pre-hypertensive) and 50 (hypertensive). Exclusion criteria were hypertension history, use of anti-hypertensive medication, renal failure, thyroid disorders, congestive heart failure, cirrhosis of the liver, liver tumors, hepatitis, use of hepatotoxic drugs, previous myocardial infarction or coronary artery bypass graft operation, coronary artery disease history, obstructive sleep apnea syndrome, biliary obstruction, alcohol abuse, and serum levels more than two-fold the upper limit of the reference value of hepatic enzymes.

### *Blood pressure measurement*

Each subject was identified with name age and sex. The systolic and diastolic blood pressures were measured 3 times using a mercury sphygmomanometer according to the American Heart Association and JNC7 (joint national committee) criteria, and the 3 measurements were averaged.[6]

### *Blood analysis*

Three ml of blood sample was collected by venipuncture for serum GGT and stored at 2-8 °C until analysis. Serum GGT was estimated by IFCC standardized method (enzymatic colorimetric assay) and reading was taken from autoanalyser (Cobas C311).

### *Ethical approval*

The ethical approval was taken from Institutional Review Committee of Nepal Health Research Council and all patients gave written consent for the study.

### *Statistical analysis*

Data were entered in excel and presented in the form of mean±SD. Statistical analysis was done by SPSS version 20. ANOVA test was applied to compute the mean difference between the groups. Pearson correlation test was applied to observe the correlation between variables. P value <0.05 was considered statistically significant.

## RESULTS

A total of 150 subjects were recruited among them, 50 patients with hypertensive disorder, 50 with pre-hypertensive disorder and 50 were healthy control. The baseline clinical characteristics of subjects are summarized in Table 1. There was no statistically significant difference for age between the groups. The body mass index (BMI) between the group is significantly different (BMI: normotensive 23.7±0.76 vs pre-hypertensive 24.8±1.3 vs hypertensive 27.3±2.1 kg/m$^2$; p=0.001).

The mean GGT activity among group is significantly different. The GGT activity of hypertensive patients is higher than pre-hypertensive patients (37.2±9.3 vs 26.8±7.9 U/l; p=0.001). Similarly the GGT activity of pre-hypertensive patients is significantly higher than normotensive participants (26.8±7.9 vs 10.3±4.6 U/l; p=0.001). Correlation of GGT with hypertension is shown is Figure 1. We found a significant positive correlation between GGT activity and BMI (r=0.3; p=0.0001).

**Table 1: Baseline parameters of the study.**

| | Normotensive (n=50) | Pre-hypertensive (n=50) | Hypertensive (n=50) | P value |
|---|---|---|---|---|
| **Age** | 41.2±6.5 | 42.3±6.4 | 42.8±6.6 | 0.128 |
| **Systolic BP (mm Hg)** | 113.2±3.8 | 129.6±4.5 | 155.8±9.1 | 0.001 |
| **Diastolic BP (mm Hg)** | 72.6±6 | 84.9±2.3 | 98.7±7.1 | 0.001 |
| **BMI (kg/m$^2$)** | 23.7±0.76 | 24.8±1.3 | 27.3±2.1 | 0.001 |
| **GGT (U/l)** | 10.3±4.6 | 26.8±7.9 | 37.2±9.3 | 0.001 |

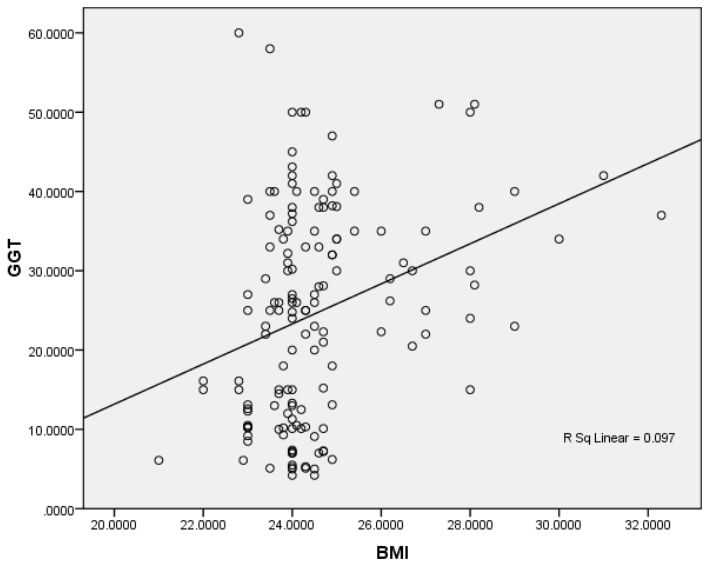


**Figure 1: Correlation between BMI (kg/m$^2$) and GGT (U/l).**

## DISCUSSION

To the best of our knowledge, this is the first study evaluating the activity of serum GGT among hypertensive patients in Nepal. Our findings showed that the level of GGT was increased among hypertensive patients. This study demonstrated an increased serum GGT activity in prehypertensive and hypertensive patients as compared to normotensive subjects. In concordance to our study Karakurt et al also found increased GGT activity among pre-hypertensive patients than normal one.[7] In the same way study conducted by Xuzen et al showed increased risk of hypertension in Korean population having higher GGT activity.[8] Similarly Lee et al demonstrated that serum GGT is a strong predictor of incident diabetes and hypertension, even within a range regarded as physiologically normal.[9] In line with these data, Sundvall et al found that the higher serum GGT level within the normal range associated with a greater intima-media thickness of the aorta.[10]

Serum GGT levels are implicated in increased blood pressure and independent predictor of risk. In recent years, GGT activity has been accepted as a valuable marker of oxidative stress. One of the suggested mechanisms for this association is the increased transport of glutathione into cells by increased GGT activity, to counteract oxidative stress by breaking down extracellular glutathione and making its component amino acids available to the cells.[11]

Glutathione is a major thiol containing molecule which plays pivotal role in cellular metabolism. It is the most potent antioxidant to maintain the redox state of mammalian cells.[12] Although GGT can be produced by different tissues throughout the body, sugar moieties linked to the enzyme display differences between the sites. Only GGT produced by the liver have major contribution in serum for detection. Since serum GGT mainly comes from the biliary system, it is a well-established serum marker for alcohol related liver disease.[7] However, there are many other reasons for an increased serum GGT level, such as congestive heart failure, stroke, hepatitis, type-2 diabetes, and metabolic syndrome.[13]

There is a growing body of evidence showing the association of GGT with atherosclerosis, diabetes mellitus, hypertension and stroke. We also found significant positive correlation between BMI and GGT. Similar to our study Choi et al showed liver enzyme including GGT were elevated in obese patients. Among the obese patients, those with fatty liver showed significantly increased GGT activity.[14] Another study conducted by Elshorbagy et al shows positive association of GGT with BMI and adiposity.[15] Salvaggio et al reported increased enzyme activity with an increase in BMI, being greater in subject with higher BMI (>30 kg/m$^2$).[16] The mechanism linking elevated GGT and obesity is still unclear. However the possible cause may be attributed to obesity. During process of obesity increased number adipose tissue may cause generalized inflammation by producing inflammatory cytokines. Circulating mediators of inflammation participate in the mechanisms of vascular insult and atheromatous change, and many of these inflammatory proteins are secreted directly from adipose tissue. This condition is accompanied by increased oxidative stress in body leading to higher activity of GGT.[14,16,17]

## CONCLUSION

Serum GGT activity is raised in prehypertensive and hypertensive participants as compared to normotensive. The elevated GGT level in hypertensive individuals

support the idea that these patients are under oxidative stress. Thus GGT may be used to assess the status of hypertension and its related complications.

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