

Status of Serum Gamma Glutamyl Transpeptidase and Serum Homocysteine in Young Adults with Essential Hypertension

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ABSTRACT

Background: Hypertension is recognized as the most common cause of cardiovascular disorder and a leading cause of morbidity and mortality in both developed and developing countries. Gamma-glutamyl transpeptidase is serum transferase enzyme synthesised by liver. It is commonly used in clinical practice to monitor liver function, hepato-biliary disorders and as a marker of alcohol intake. It has been proposed that gamma glutamyl transpeptidase is a potent preclinical marker of atherosclerosis. Hyperhomocysteinemia (HHcy) has been regarded as a new risk factor related to hypertension. Our study was aimed to find out the status of serum gamma glutamyl transpeptidase and homocysteine in hypertensive and normotensive subjects & Correlation of serum GGT with serum homocysteine in hypertensive subjects.

Materials and methods: The present study was conducted on 100 patients with essential hypertension who attended the medical OPD of Jawahar Lal Nehru Medical College and Associated Group of Hospital, Ajmer. The results of patients were compared with 50 normotensive subjects. Anthropometric parameters and biochemical estimation were performed after taking approval from Ethical Committee. The Serum GGT was measured by colorimetric kinetic assay and Serum Homocysteine was measured by ELISA technique.

Results: The mean serum level of GGT was elevated in hypertensive subjects as compared to normotensive subjects (controls) and was statistically significant ($P < 0.001$). The mean serum level of Homocysteine was elevated in hypertensive subjects as compared to normotensive subjects and was highly significant ($P < 0.0001$). The present study has also shown a positive correlation ($r = 0.74$) between serum GGT

& serum homocysteine in hypertensive subjects.

Conclusion: The present study shows that the level of both, serum GGT and serum homocysteine is raised in young adult patients with essential hypertension and has also shown a positive correlation between serum GGT & serum homocysteine in these subjects. Thus the elevated GGT and Homocysteine in young adults may contribute to their susceptibility to hypertension and provide an additional evidence of novel role of GGT and Homocysteine in cardiovascular risk evaluation. This study was limited and needs to be further worked upon.

Keywords: Homocysteine (Hcy), Hypertension (HTN), Hyperhomocysteinemia (HHcy), Serum γ -glutamyl transpeptidase, Serum γ -glutamyl transferase (GGT).

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INTRODUCTION

Hypertension is defined as blood pressure of equal to or greater than 140/90 mmHg has been recognized as the most common cause of cardiovascular disorder and a leading cause of morbidity and mortality in both developed and developing countries.¹⁻³ Essential hypertension has been appropriately called the silent killer because it is usually asymptomatic and undetected. Uncontrolled hypertension can cause damage to all organs of body.⁴ Essential hypertension is increasing rapidly among young generation due to changes in dietary habits and lifestyle modifications.⁵ Premature death in young adults is mainly due to cardiovascular diseases. Therefore it is very essential to diagnose and treat hypertension as early as possible.⁶

Recent research has revealed that GGT is a pro inflammatory marker involved in atherosclerosis leading to Hypertension. GGT is an important enzyme which maintains the steady state

concentration of glutathione both inside cells and the extracellular fluids. GGT is a glycoprotein consisting of two polypeptide chains.^{7,8} Gamma-glutamyl transpeptidase, initially used as an indicator of liver function is now found to be elevated in other metabolic disorders like non-insulin dependent diabetes mellitus, Hypertension etc.⁹

Glutathione is a tripeptide, composed of Glutamic acid, Glycine and Cysteine.^{10,11} The main function of GGT is to degrade glutathione to form a dipeptide which act as a reducing agent and forms free radicals.¹² These free radicals oxidise LDL and forms a plaque in endothelial lining of the blood vessels. Progressive formation of plaque results in atherosclerosis leading to hypertension and cardiovascular disease.¹³ The relationship between hyperhomocysteinemia and atherosclerosis was suggested by McCully (1969).¹⁴

Hyperhomocysteinemia is a medical condition generally defined as Serum Homocysteine level ≥ 15 $\mu\text{mol/L}$. Hyperhomocysteinemia (HHcy) has been regarded as a new risk factor related to hypertension.¹⁵⁻¹⁸ Homocysteine is a sulfur-containing amino acid and an intermediate in the methionine metabolism. It is recycled either by trans-sulfuration to cysteine or by remethylation to methionine and is mainly cleared through the kidneys.^{19,20}

Numerous nutritional deficiencies (folate, vitamins B₁₂ and B₆, act as cofactors in methionine metabolism), genetic variation (mutation of methylene tetra- hydrofolate reductase enzyme.), drugs (phenytoin, carbamazepine), or diseases (renal insufficiency) affect homocysteine metabolism and influence serum homocysteine levels.²¹ Homocysteine contains a reactive sulfhydryl group that can react with plasma constituents and promotes oxidative damage. Hyperhomo cysteinemia, through its oxidative effects, could reduce vasodilators like nitric oxide as well as promote extracellular matrix accumulation and smooth muscle cell proliferation, leading to vascular constriction and stiffness.^{22,23} An elevated homocysteine level therefore induces thrombogenicity, causes procoagulant state and promotes the proliferation of smooth muscle cells.²⁴

Epidemiological studies demonstrated that both hyperhomocysteinemia and hyper- tension were related to an increased risk of cardiovascular events.^{16,25} In a large epidemiological study (NHANES III) each $5\mu\text{mol/L}$ increase in plasma Homocysteine levels was associated with an increase in systolic (SBP) and diastolic blood pressure (DBP) of 0.7 and 0.5 mmHg, respectively, in men, and 1.2 and 0.7 mmHg, respectively, in women.²⁶

However, the effect of homocysteine lowering interventions seemed to be paradoxical in the hypertensive population. Nutritional supplements could lower homocysteine levels in most studies, but this was not always related to blood pressure.^{27,28}

Our study was aimed to find out the status of serum gamma glutamyl transpeptidase and homocysteine in hypertensive and normotensive subjects & Correlation of serum GGT with serum homocysteine in hypertensive subjects. There is not a lot of study that shows relation between serum GGT and serum homocysteine in hypertensive subjects.

MATERIALS AND METHODS

The present study is a case control study, 100 subjects with Essential hypertension (group-2) and 50 age and sex matched healthy controls (group-1) both male and female between 30 -50 years of age were recruited from Jawahar Lal Nehru Medical College and Associated Group of Hospital, Ajmer. The present study is approved by institutional ethical committee.

Exclusion criteria

Pregnant, lactating women and patients with diabetes, liver disease and patients on drugs which might influence the serum levels of GGT and Homocystiene were excluded from the study. Height and weight were measured with the subject in light clothes without shoes, and BMI was calculated by using the formula: [BMI = weight (Kgs) /height (metre)²]

Blood pressure (BP) was measured by physician. 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.²⁹

Blood samples were collected after an overnight fast (12-14hrs) under aseptic conditions from all the study participants. All samples were centrifuged and analyzed for serum GGT and Serum Homocysteine. The Serum GGT was measured by colorimetric kinetic assay and serum Homocysteine was measured by ELISA technique.

Statistical analysis: All data were analysed by SPSS-13 version. $P < 0.01$ were considered as significant.

Table 1: Anthropometric Parameters of Normotensive v/s Hypertensive Subjects

PARAMETERS	NORMOTENSIVE SUBJECTS n = 50	HYPERTENSIVE SUBJECTS n =100	P VALUE
Age (yrs)	39.84 \pm 6.04	42.53 \pm 5.49	> 0.005
Height (cm)	156.08 \pm 7.19	150.18 \pm 5.4	< 0.001
Weight (kg)	60.16 \pm 10.19	67.72 \pm 8.17	< 0.001
BMI (Kg/m ²)	21.75 \pm 2.6	26.6 \pm 2.9	< 0.001

Table 2: Biochemical Parameters of Normotensive v/s Hypertensive Subjects

BIOCHEMICAL PARAMETERS	NORMOTENSIVE SUBJECTS n =50	HYPERTENSIVE SUBJECTS n=100	P VALUE
GGT (U/L)	34.5 \pm 8.4	53.39 \pm 16.09	<0.001
SERUM HOMOCYSTEINE ($\mu\text{mol/l}$)	10.06 \pm 2.9	18.97 \pm 4.5	<0.0001

RESULTS

A total of 150 subjects were studied. The results are summarized in Tables and Figures. The Table-1, Figure-1 shows the Mean \pm SD of age, weight, height and body mass index of the subjects. The Table-2, Figure-2 shows the Mean \pm SD of serum GGT (53.58 \pm 16.09 v/s 34.5 \pm 8.4)U/L in hypertensive subjects compared to normotensive subjects (controls) was significantly

($P < 0.001$) raised and the Mean \pm SD of Serum Homocysteine (18.97 \pm 4.5v/s 10.06 \pm 2.9) $\mu\text{mol/l}$ in hypertensive subjects compared to normotensive subjects was highly significant ($P < 0.0001$). Figure-3 shows positive correlation ($r = 0.74$) between serum GGT and serum Homocysteine levels in Hypertensive subjects.

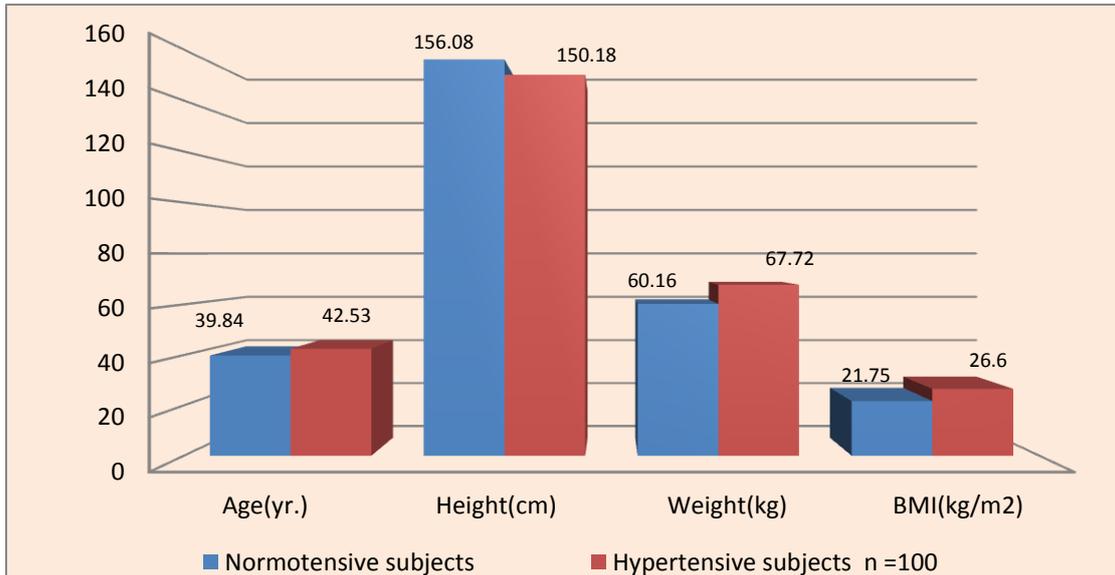


Fig 1: Comparison of Anthropometric Parameters of Normotensive v/s Hypertensive Subjects

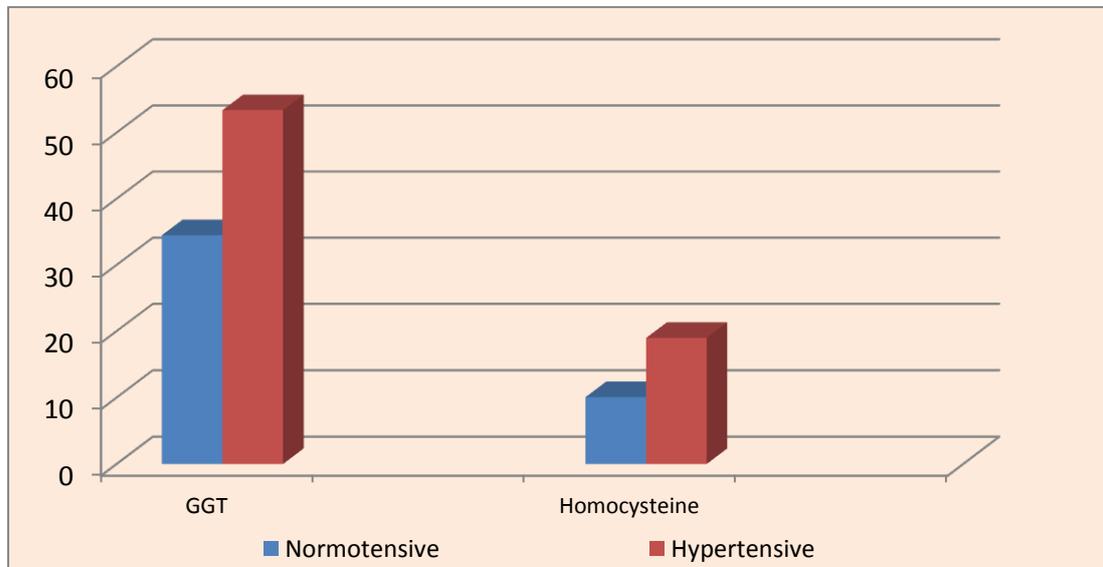


Fig 2: Comparison of Biochemical Parameters of Normotensive v/s Hypertensive Subjects

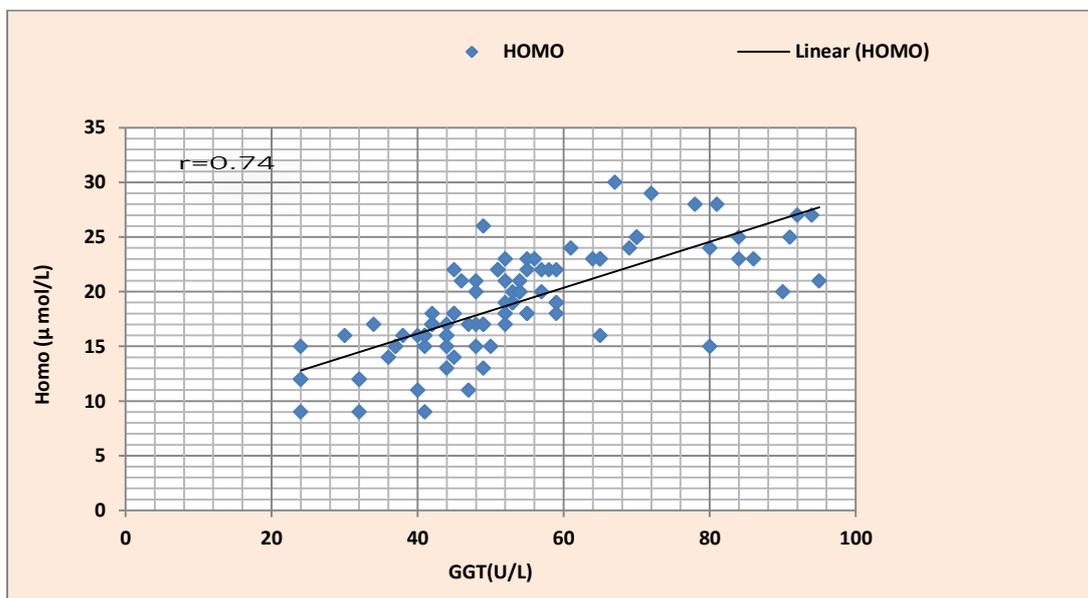


Fig 3: Correlation of Serum GGT with Serum Homocysteine in Hypertensive Subjects. (n=100)

DISCUSSION

Elevated blood pressure is a significant strong and independent risk factor for coronary artery disease both in men and women. In the present study we have observed that the level of serum GGT was elevated in hypertensive subjects as compared to the normotensive subjects. It is in concordance with the previous studies which also state that the serum GGT was elevated in hypertensive subjects [29-33]. Our finding are in agreement with Raja Rajeshwari D et al. (2015) reported that the level of serum GGT (70.10 ± 25.08 v/s 23.34 ± 8.42) in hypertensive subjects was highly significant than normotensive subjects.³³ In the present study we have also observed that the level of serum homocysteine was elevated in hypertensive subjects as compared to the normotensive subjects. Our finding are in agreement with Alina et al. (2008) found that the value of serum homocysteine ($18.77 \pm 1.9 \mu\text{mol/l}$) in hypertensive subjects was highly significant than normotensive subjects.³⁴ Drzewoski et al. (2000) reported that elevated blood levels of homocysteine is strongly related to an increased risk for atherosclerosis and cardiovascular disease.³⁵ Our study also shows positive association between serum GGT and serum Homocysteine levels in hypertensive subjects. Plasma GGT has been suggested as a marker of oxidative stress, a risk factor of hypertension and cardiovascular diseases.^{36,37} GGT is a key enzyme in the catabolism of glutathione and plays a role in the production of reactive oxygen species. HHcy causes vascular dysfunction mainly through its oxidative effects, which could reduce vasodilators like nitric oxide as well as promote extracellular matrix accumulation and smooth muscle cell proliferation, which could lead to vascular constriction and stiffness.^{22,23} Increase in plasma concentration of homocysteine is common in patients with stroke, peripheral vascular disease³⁸ and coronary disease³⁹ and confer an independent risk of atherosclerosis.⁴⁰

CONCLUSION

The present study shows that the level of both, serum GGT and serum homocysteine is raised in young adult patients with essential hypertension and has also shown a positive correlation between serum GGT & serum homocysteine in these subjects. Thus the elevated GGT and Homocysteine in young adults may contribute to their susceptibility to hypertension and provide an additional evidence of novel role of GGT and Homocysteine in cardiovascular risk evaluation. This study was limited and needs to be further worked upon.

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