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A CORRELATIVE STUDY OF SERUM GAMMA-GLUTAMYL TRANSPEPTIDASE WITH SERUM LIPID PROFILE IN YOUNG ADULT HYPERTENSIVE PATIENTS IN INDIAN POPULATION

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ABSTRACT

Background: Hypertension and dyslipidemia are major risk factors for cardiovascular disease (CVD) and account for more than 80% of deaths and disability in low and middle-income countries. Gamma-glutamyl transpeptidase is serum transferase enzyme synthesised by liver. GGT initially used as an indicator of alcohol ingestion is now viewed as a sensitive marker of sub clinical inflammation. Our study was aimed to find out the status of serum GGT and serum lipid profile in hypertensive and normotensive subjects & correlation of serum GGT with serum lipid profile 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 para- meters and biochemical estimation were performed after taking approval from Ethical Committee. The serum total cholesterol (TC), triglyceride (TG) and HDL cholesterol (HDL-C) were determined enzymatically, while LDL cholesterol (LDL-C) was calculated using the Friedewald formula & serum GGT was measured by colorimetric kinetic assay. **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 values of serum TC, TG and LDL-C were significantly higher and statistically significant among the hypertensive patients compared to normotensive subjects & the mean HDL –C level was lower in the hypertensive subjects compared to normo- tensive subjects and was statistically significant. The present study has also shown the positive correlation between serum GGT and serum TC, TG and LDL-C & negative correlation between serum GGT and HDL-C in hypertensive subjects. **Conclusion:** The observations of this study have revealed that there was significant alteration of serum GGT, cholesterol, triglyceride, HDL cholesterol and LDL cholesterol in hypertensive patients. GGT can be used a potent biochemical marker for preclinical development of atherosclerosis. Therefore, for routine monitoring of hypertensive patients to prevent the coronary heart disease (CHD) and other consequences, the reinforcement of these parameters may be recommended in daily clinical practice. This study was limited and this topic needs to be further worked upon.

KEYWORDS : Cardiovascular disease (CVD), Gamma-glutamyl transferase (GGT), Total cholesterol (TC) , Triglyceride (TG), HDL cholesterol, LDL cholesterol.

INTRODUCTION

Hypertension and dyslipidemia are major risk factors for cardiovascular disease (CVD) and account for more than 80% of deaths and disability in low and middle-income countries (1, 2). Essential hypertension is increasing rapidly among young generation due to changes in dietary habits and lifestyle modifications (3). The most important risk factors for the development of hypertension are increased salt intake, obesity, cigarette smoking, elevated serum level of cholesterol and triglyceride , lack of physical exercise, genetic factors , stress and strain (4). GGT is an enzyme that transfers gammaglutamyl functional groups. It is present in kidney, lymphocytes, lungs, brain etc with predominance in liver (5). It is commonly used in clinical practice to monitor liver function, alcohol consumption and hepatobiliary disorders (6). Recently it has been proposed that GGT is a potent biochemical marker for preclinical development of atherosclerosis (7,8). It may affect lipid metabolism leading to hypercholesterolaemia and hypertriglyceridemia (9,10). The proposed mechanism of GGT was to catalyzes the initial step in the extracellular degradation of antioxidant glutathione, which results in the amino acids cysteine and glycine. The reactive thiol of cysteinyl –glycine generates superoxide anion radicles and hydrogen peroxide through its interaction with free iron. These GGT mediated reactions have been shown to catalyze oxidation of low density lipoprotein, which may contribute to oxidative events influencing plaque evolution and rupture (11). An excessive daily intake of saturated fats, cholesterol, other sources of calories and subsequent disturbance of lipid profile leading to hypertriglyceridemia and hypercholesterolemia are associated with obesity and consequently, hypertension (12, 13). Epidemiological studies have established a strong association between hypertension and coronary artery disease (14). Indians have been reported to have the highest incidence of CAD (15).

Serum GGT activity is affected by genetic and enviormental factors with heritability estimated at 0.52 . The study by Michele Emdin et al. found positive correlation of GGT with total cholesterol, Triglyceride, LDL- cholesterol in myocardial infarction Patients (16).

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. Anthropometric para- meters and biochemical estimation were performed after taking approval from Ethical Committee. The serum total cholesterol (TC), triglyceride (TG) and HDL cholesterol (HDL-C) were determined enzymatically, while LDL cholesterol (LDL-C) was calculated using the Friedewald formula & serum GGT was measured by colorimetric kinetic assay.

Exclusion criteria: Pregnant, lactating women and patients with diabetes, liver disease and patients on drugs which might influence the serum levels of lipid profile and GGT 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 a 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 (17). Serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), and triglyceride (TG) levels were classified on the basis of the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III) (18). Elevated TC was defined as having TC levels of (>200 mg/dL), Low HDL-C was defined as having HDL-C levels of (< 40 mg/dL) elevated LDL-C was defined as having LDL-C levels of (>130 mg/dL), Elevated TG was defined as having triglyceride levels of (>150 mg/dL). 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 lipid profile and serum GGT. The Serum Total cholesterol, triglyceride and HDL cholesterol were determined enzymatically, while LDL cholesterol was calculated using the Friedewald formula & Serum GGT was measured by colorimetric kinetic assay.

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

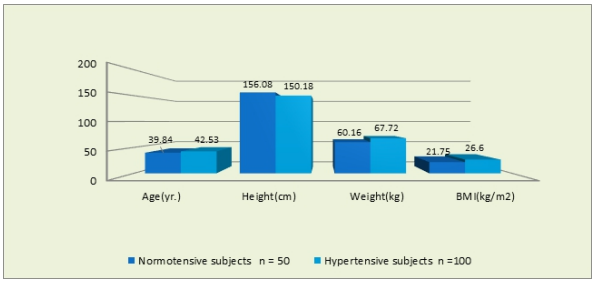
Results: A total of 150 subjects were studied. The results are summarized in Tables and Figures. The Table-1, Figure-1 shows that the Mean±SD of weight and BMI were more in hypertensive patients than normotensive and the difference was significant (P<0.001) while the mean age was not significant (P>0.005). The Table-2, Figure-2 shows the Mean ± SD of serum GGT (53.58 ± 16.09 v/s 34.5 ± 8.4) U/L in hypertensive subjects compared to normotensive subjects (controls) was significantly (P<0.001) raised. The Table-2, Figure-2 also shows that the level of serum TC (223.13 ± 53.05 v/s 162.04 ± 34.01) mg/dl, serum TG (175.95±75.26 v/s 120.02±18.02) mg/dl, and serum LDL-C (148.06±56.53v/s 92.76±16.5) mg/dl, in hypertensive patients compared to normotensive were significantly (P<0.001) raised while serum HDL-C (40.07±6.5 v/s 50.06±9.7) mg/dl in hypertensive patients compared to normotensive was decreased significantly (P<0.001). The serum GGT showed positive correlation with TC (r=0.76) (Figure-3), TG (r = 0.71) (Figure-4), LDL-C (r=0.76) (Figure-6) and negative correlation with HDL-C (r=-0.62) (Figure-5) in hypertensive subject.

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 ± 6.04	42.53 ± 5.49	> 0.005
Height (cm)	156.08 ± 7.19	150.18 ± 5.4	< 0.001
Weight (kg)	60.16 ± 10.19	67.72 ± 8.17	< 0.001
BMI (Kg/m2)	21.75 ± 2.6	26.6 ± 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 ± 8.4	53.39±16.09	<0.001
Total Chol. (mg/dl)	162.04 ± 34.01	223.13 ± 53.05	<0.001
Triglyceride (mg/dl)	120.02 ± 18.02	175.95± 75.26	<0.001
HDL-C (mg/dl)	50.06 ± 9.7	40.07 ± 6.5	<0.001
LDL-C (mg/dl)	92.76 ± 16.5	148.06 ± 56.53	<0.001



Fig– 1 Comparision of Anthropometric Parameters of Normotensive v/s Hypertensive Subjects

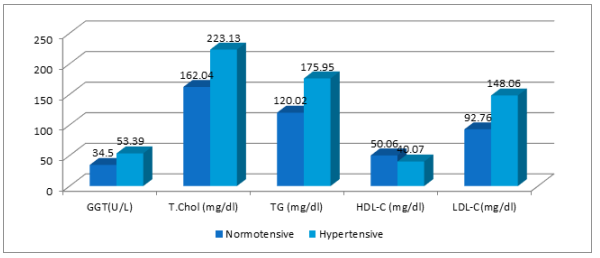


Fig-2 Comparision of Biochemical Parameters of Normotensive v/s Hypertensive Subjects

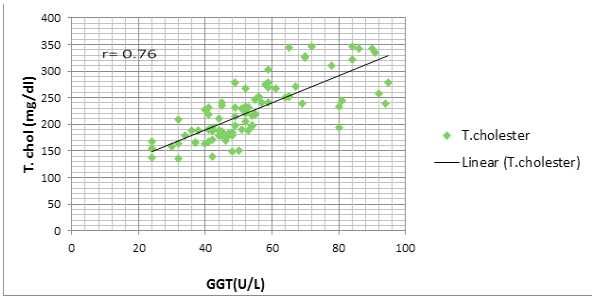


Fig-3 Correlation of Serum GGT With Total Cholesterol in Hypertensive subjects (n=100).

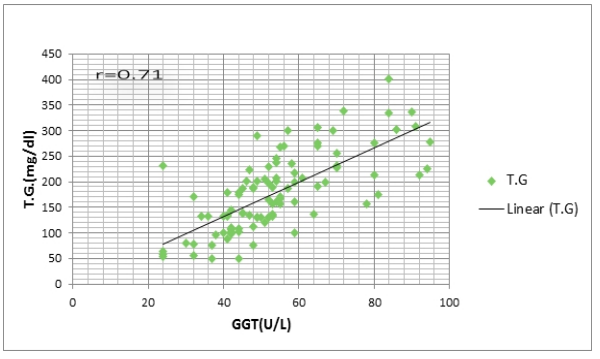


Fig-4 Correlation of Serum GGT With Triglyceride in Hypertensive Subjects (n=100).

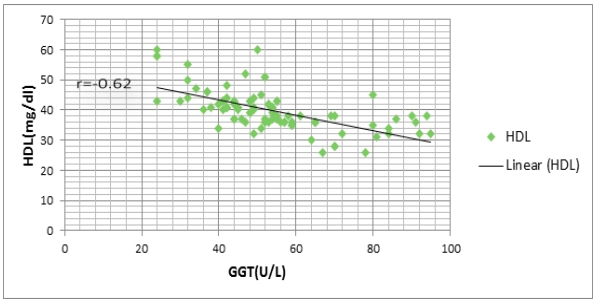


Fig-5 Correlation of Serum GGT With HDL-Cholesterol in Hypertensive subjects (n=100).

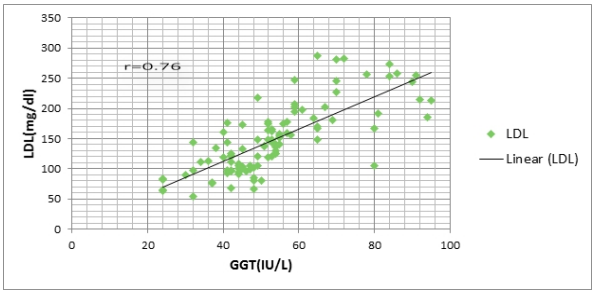


Fig-6 Correlation of Serum GGT With LDL-Cholesterol in Hypertensive Subjects (n=100).

Discussion

Hypertension and dyslipidemia are major risk factors for cardiovascular disease (CVD) and a leading cause of morbidity and mortality in both developed and developing countries

GGT 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. Recent clinical studies have shown its association with blood pressure and lipid profile. Plasma GGT has been suggested as a marker of oxidative stress (19, 20) a risk factor of hypertension and cardiovascular diseases. The main function of GGT is to degrade glutathione to form a dipeptide which act as a reducing agent and forms free radicals (21). 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 (22).

In the present study we have observed that the level of serum GGT was elevated in hyper-tensive 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 (23, 24, 25, 26, 27).

Results of our study revealed that the mean values of serum TC TG and LDL-C were significantly higher and statistically significant among the hypertensive patients compared to normotensives. The mean HDL-C level was lower in the hypertensives compared to normotensives and was statistically significant.

It is in concordance with the previous studies which also state that mean values of serum TC, serum TG and serum LDL-C were significantly higher and statistically significant among the hypertensive patients compared to normotensies (28, 29, 30, 31). According to Pavithran et al. alteration in lipid metabolism including a decrease in HDL-C can result in endothelial damage and trigger an increase in blood pressure which may partially account for its strong predictive power for CHD (32). The present study has also shown the positive correlation between serum GGT and total cholesterol, Triglyceride, LDL- cholesterol & negative correlation between serum GGT and HDL cholesterol in hypertensive subjects. It is in concordance with the previous studies which also state that the positive correlation between serum GGT and total cholesterol, Triglyceride, LDL- cholesterol & negative correlation between serum GGT and HDL cholesterol in hypertensive subjects (27).

Conclusion: The observations of this study have revealed that there was significant alteration of serum GGT, cholesterol, triglyceride, HDL cholesterol and LDL cholesterol in hypertensive patients. GGT can be used a potent biochemical marker for preclinical development of atherosclerosis. Therefore, for routine monitoring of hypertensive patients to prevent the coronary heart disease (CHD) and other consequences, the reinforcement of these parameters may be recommended in daily clinical practice. This study was limited and this topic needs to be further worked upon

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