Original Article

Comparison of Liver Enzymes and Cardiovascular Risk Factors in Hypertensive and Normal Subjects

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ABSTRACT

Objective: To compare the liver enzymes between hypertensive and normal subjects.

Study Design: Cross-sectional, descriptive study.

Place and Duration of Study: Basic Medical Sciences Institute, J.P.M.C, Nehal Hospital and Shamsi Hospital Karachi, from December 2006 to March 2011.

Materials and Methods: The study has compared the liver enzymes and associated cardiovascular risk factors like blood pressure, BMI, waist hip ratio, blood sugar, lipid profile between 100 normal and 100 hypertensive subjects. The assessment was done by applying independent t test and Pearson correlation using statistical package for social sciences 15.

Results: The normal and hypertensive subjects were compared with liver enzymes, systolic and diastolic blood pressure, lipid profile, BMI and waist/hip ratio. All values showed significant correlation ($P < 0.001$) using independent t test. In the hypertensive subjects all the liver enzymes were found to be raised in comparison with hypertensive but were within their normal ranges. The levels of GGT (Gamma glutamyl transferase) was found to be raised beyond its normal range and was compared according to type I and Type II stage of hypertension and was found to be raised significantly.

Conclusion: Among all the liver enzymes compared with uncontrolled hypertensive GGT was found to be most significantly correlated with all the factors increasing cardiovascular risk, and needs to be measured in every hypertensive individual.

Key Words: Blood pressure. Gamma Glutamyl transferase. Cardiovascular risk factors.

INTRODUCTION

The prevalence of cardiovascular disease and its associated risk factors are increasing worldwide. The recent data collected showed that about one quarter of the worlds population is hypertensive and around 1.15 billion hypertensive patients will be in developing world by 2025 [1].In south Asia the prevalence of cardiovascular disease and its adverse health effects are increasing far more rapidly than in young age group in any other region of the world [2, 3].The main associated risk factors which are linked to this high prevalence are hypertension, diabetes mellitus and obesity.[4]

Gamma- glutamyltransferase (GGT) has always been used as a marker to assess the excessive alcohol intake,[5] It has been recently linked with cardiovascular disease and all cause mortality, suggesting its role as predictor of cardiovascular disease [6]. The role of GGT in cardiovascular risk factor such as dyslipidaemia,[7] hypertension,[8] diabetes mellitus and metabolic syndrome[9] irrespective of alcohol consumption. However the exact mechanism linking GGT with cardiovascular disease is still lacking. Although lot of data on various aspects of hypertension and liver enzymes has been published in western world, very few if any such study has taken place in this part of the world. In this study we aim to evaluate the levels of liver enzymes in general and GGT in particular with hypertension and its associated risk factors. The studies also compare liver enzymes in normal subjects.

MATERIALS AND METHODS

The study was conducted in the Department of Physiology, B.M.S.I., J.P.M.C, Karachi and secondary care hospitals of Karachi Nehal General Hospital Malir Kala Board Karachi and Shamsi General Hospital Shamsi society near wireless gate Karachi. The study was done initially from December 2006 to 2008 and was then further extended to March 2011.

The present study was cross-sectional study, 100 normal subjects and 100 hypertensive subjects were selected. The inclusion criteria was adult with either gender above 18 years of age. The hypertensive subjects were included by measuring blood pressure or if they were on anti-hypertensive therapy. Subjects with acute or chronic liver, kidney and heart disease, history of alcohol addiction, patients taking drugs affecting liver enzymes, patients suffering from cancer, and pregnant women. Subjects with hepatitis C virus antibody and hepatitis B virus surface antigen and patients with aspartate amino transferase (SGOT) and alanine amino transferase (SGPT) and Gamma Glutamyltransferase (GGT) levels more than three times normal and subject with total leukocyte count more than 10,000/µl were excluded. Hypertension was

defined according to the criteria set by JNC VII classification of hypertension.[8]

A verbal consent of the patients were taken at JPMC and written informed consent of the patients were taken at Nehal and Shamsi hospital. The protocols of the procedure were explained before taking the sample. All participants were asked to fast at least 12 hours and take their medications with their evening meal. They are also instructed to avoid heavy physical activity for at least 2 hours before examination. Height and weight was measured with the help of height and weight scale ZT-120. Weight was measured in standing position without shoes while the shoulder was in normal position. BMI was calculated as weight in kilograms divided by height in meters square. Among the measurements of abdominal obesity, high waist circumference was defined > 90 cm in males and > 80 cm in females. After a 5 minute rest blood pressure was measured in sitting position. History of daily physical activity, addiction, previous illnesses and types of medication use was also noted. Reference range of values, in our laboratory, are 0–40 IU/l for ALT, 0–37 IU/l for AST, 0–50 IU/l for GGT. High cholesterol (TC), high triglyceride (TG), high low density lipoprotein cholesterol (LDL), and low high density lipoprotein cholesterol (HDL) were defined as TC ≥ 200 mg/dl,TG ≥150 mg/dl, LDL-C ≥ 130mg/dl, and HDL-C ≤ 40 mg/dl according to ATP III.[9]Eight milliliter of venous blood was drawn with a disposable syringe. Two milliliter was transferred to EDTA containing tube for CBC and remaining blood was stored for collection of serum. Complete Blood Count was done by Automated cell counter SYSMEX KX 21. Blood sugar was done by GOD-PAP Enzymatic Colorimetric Method. Tests for the detection of liver enzymes were performed on Microlab 300 Merck by enzyme kinetic method, the kit by Bioscience (Spain) were used. Hepatitis C virus antibodies are detected by chromatographic immunoassay (LG Quick card). Hepatitis B surface antigen is detected by qualitative immunoassay (Abbot Laboratory).

Statistical Analysis: Data analysis was done on Statistical Package for Social Sciences (SPSS) version 15. The statistical significance of difference between the mean values of two groups was evaluated by the students't' test. The difference in the mean values of the two groups was regarded as statistical significant if the P value was less than 0.05 and it was taken as highly significant if P value was less then 0.001. Correlation Coefficient was detected using Pearson coefficient of correlation SPSS-15. Figure was computed on Microsoft excel 2007.

RESULTS

The study included 100 uncontrolled hypertensive and 100 normal subjects consisting of 93 female and 107 male. Table I is shows the comparison of physical parameters between normal and hypertensive groups. The table has shown that patients who were hypertensive have increased levels of GGT with increased waist hip ratio and BMI.

Table No.1: Comparison of Physical Parameters in Normal and Hypertensive

Category	Group	Mean ± Std Deviation	P value
BMI kg/m^2	Control	21.21±1.49	0.000**
	Hypertensive	25.66±1.92	
w/h ratio	Control	0.92±0.27	0.000**
	Hypertensive	0.98±0.58	
Systolic Blood pressure mm of Hg	Control	121.46±10.66	0.000 **
	Hypertensive	163.37±9.81	
Diastolic Blood Pressure mm of Hg	Control	77.91±7.21	0.000 **

n = 100 control subjects and 100 hypertensive subjects (** P = < 0.001, * = < 0.05)

Table No.2: Comparison of Biochemical Parameters in Normal and Hypertensive

Category	Group	Mean ± Std Deviation	P value
FBS mg/dl	Control	88.92±12.29	0.04 *
	Hypertensive	94.24±13.69	
RBS mg/dl	Control	121.46±14.6	0.000 **
Total lipid mg/dl	Control	681.04±54.76	
	Hypertensive	945.10±188.15	
Cholesterol mg/dl	Control	179.46±16.43	0.000 **
	Hypertensive	256.39±62.17	
Triglycerides mg/dl	Control	160.76±12.46	0.000 **
	Hypertensive	216.16±53.89	
HDL mg/dl	Control	42.67±3.67	0.000 **
	Hypertensive	33.63±2.99	
LDL mg/dl	Control	113.44±11.94	0.000 **
	Hypertensive	207.32±47.55	
Creatinine mg/dl	Control	0.87±0.080	0.000 **
	Hypertensive	1.15±0.100	
SGPT IU/L	Control	8.53±1.77	0.000**
	Hypertensive	20.81±12.72	
SGOT IU/L	Control	7.78±1.36	0.000 **
	Hypertensive	10.55±1.56	
GGT IU/L	Control	17.58±6.02	0.000 **
	Hypertensive	55.91±8.27	
ALK Phos-phatase IU/L	Control	125.80±10.33	0.070

n = 100 control subjects and 100 hypertensive subjects (** P = < 0.001, * = < 0.05)

Table 2 is shows the biochemical parameters of lipid profile and serum creatinine and liver enzymes which were found to be raised in hypertensive group when

compared with normal subjects. All the hypertensives have shown rise in lipid profile impaired or rise in blood sugar levels and increases in liver enzymes in comparison with normal subjects.The hypertensives were divided into two groups according to severity of hypertension into type I stage and Type II stage of hypertension JNC VII Fig I and II. Type I group is considered as moderate hypertensive consists of systolic > 140 to 159 mm Hg and diastolic >90 to 99 mmHg. The Type II group is considered as severe hypertensive with systolic >160 and diastolic > 100 mm Hg. The figure I and II were showing the levels of GGT in with respect to rise in blood pressure in stage I and stage II of hypertension. The mean values were compared with systolic and diastolic blood pressure respectively which showed the raised levels of GGT as the blood pressure rises.

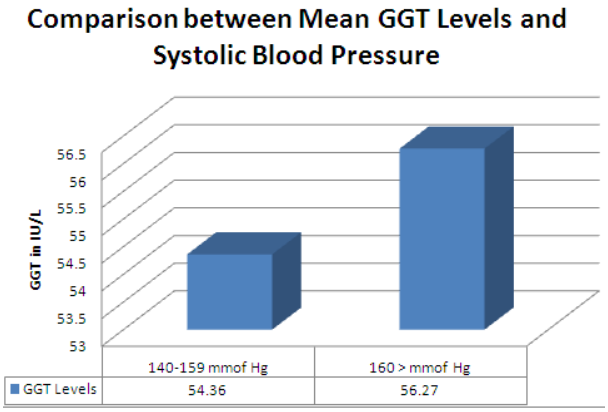

Figure No.I. Comparison of stage I and Stage II systolic blood pressure with GGT levels.

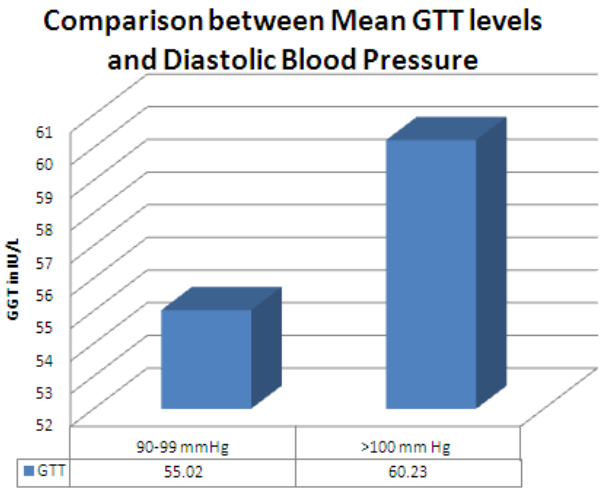

Figure No.2. Comparison of stage I and stage II Diastolic blood pressure with GGT levels.

DISCUSSION

In this study the relationship of liver enzymes with hypertension was evaluated in life time non-alcoholics in both genders. The level of liver enzymes was found to be raised when compared between normal and hypertensive subjects, but all were found to be within their normal range except GGT table I. The results of this study clearly indicate that in hypertensives have raised levels of BMI and waist hip ratio which could be one of the factors of raised levels of GGT in these patients. Similar findings were also founded by studies done elsewhere which are done on nonalcoholics.[10,11]

In this study the levels of GGT were found to be raised in hypertensives with factors favoring obesity (BMI, waist hip ratio), and cardiovascular risk factors (blood sugar, total lipid, cholesterol,triglycerides,LDL and low HDL), conforming with previous studies mainly conducted in European population or among alcoholics [12,13]

The raised levels of GGT was among overweight or individuals with increased waist hip ratio, supports the finding of previous studies [14,15] which have correlate central adiposity as a stronger predictor of elevated liver enzymes especially GGT, as our findings further support the hypothesis that NAFL may represent an important underlying mechanism for the observed associations between GGT and Hypertension. In this study the relationship between raised GGT and hypertension was further evaluated by dividing the hypertensive subjects into two groups of Type I stage and Type II stage of Hypertension[8]. Among the group with raised diastolic blood pressure the GGT was found to be significantly raised in comparison with raised sytolicblood pressure.

Arterial stiffness, which is due to change in structural and function characteristics of the vessel wall, has been related as independent predictor of cardiovascular events and mortality [16]

It is persumed that the levels of GGT in the serum may occurs in those individuals with low but persistent increase in oxidative and other cellular stresses. Many experimental studies have indicated the GGT levels are directly involved in the generation of reactive oxygen species in the presence of iron or other transition metals[17,18]. The levels of GGT activity are directly related to oxidative stress which play a leading role in the development of atheromatous plaques and produce oxidation of LDL in the presence of iron ions [19].Gamma-glutamyltransferase activity has been identified in human atheromatous plaques [20].Previous studies have also compared the levels of GGT are with some atherosclerotic risk factors and used GGT levels as a predictors of future heart disease, hypertension,and stroke [21,22.]

Although the exact mechanism responsible for this association is unknown, several possible mechanisms have been proposed for the role of serum GGT in increasing cardiovascular risk. The most widely accepted mechanism is oxidative stress, followed by hepatic insulin resistance and subclinical inflammation. Another reason of elevated serum GGT in patients with hypertension could be due to inflammation due to

atherosclerotic cardiovascular disease [23]. The oxidative processes which presumably can lead to generation of free radicals in the presence of Fe ++ and Cu++ and induce oxidative stress [24].

CONCLUSION

Our findings indicate that the association between GGT and hypertension are not related solely by alcohol consumption. Increase in levels BMI, waist hip ratio, high Cholesterol, triglycerides, LDL and low HDL (as cardiovascular risk factors) can lead to increase in GGT.

However the exact mechanism by which the levels of GGT were found to be raised in hypertension and how it increases the risk factors of cardiovascular diseases are yet to be analyzed and need further studies.

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