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A COMPARISON OF THE EFFECTS OF GAMMA GLUTAMYLTRANSFERASE ON AGE AND OBESITY AMONG NORMAL, HYPERTENSIVE AND TYPE 2 DIABETICS

AZHAR IQBAL, AKBAR KHOJA, UZMA IFTIKHAR AND MEHJABEEN
Department of Physiology, Bahria Medical and Dental College, Bahria University Karachi, Basic Medical Sciences Institute, J.P.M.C., Karachi, Hamdard College of Medicine & Dentistry, Hamdard University, Karachi - Pakistan

ABSTRACT
The purpose of this work was to compare the effects of Gamma Glutamyltransferase on age and obesity among normal, hypertensive and type 2 diabetics. It is a cross-sectional study which was conducted in the department of Physiology B.M.S.I., J.P.M.C. Karachi from December 2006 to October 2007. All subjects who have never used alcohol in their lifetime were selected. A total of 100 normal, 50 each diabetic and hypertensive patients were recruited to the study. Increase in age was significantly associated with raised GGT levels in normal, hypertensive and type 2 diabetic subjects ($p < 0.01$). GGT levels were significantly ($p < 0.001$) greater in both hypertensive and diabetic subjects compared to normal subjects. The study confirms the relation between age obesity with GGT levels among non-alcoholics. This study also indicates the significance of GGT among diabetics and hypertensive patients.

INTRODUCTION

Gamma glutamyltransferase (GGT) is present in serum and surface of most cell types, and is the enzyme responsible for initiating extra cellular catabolism of glutathione. Increased GGT activity may be a response to oxidative stress, which can increase the transport of glutathione precursors into cells[1]. Recent reports also indicate a direct role for GGT in the generation of reactive oxygen species.[2-4] In this context, emerging evidence from epidemiological studies indicates that GGT may have a role in the pathogenesis of cardiovascular disease, diabetes mellitus, and metabolic syndrome.[5] Similarly recent cross-sectional and longitudinal studies have also noted a relatively independent association between elevated serum GGT levels and hypertension.[6,7] Several groups of investigators have also emphasised obesity as an important factor, that can increase serum GGT activities.[8,9]

Age has been suggested to affect GGT activity,[10,11] however; the possible age related effects on serum GGT activities were done in association with alcoholic drinkers and among non-alcoholic drinkers. The data on life time non-alcoholics is nearly nonexistent in this country. Serum GGT activity is affected by genetic and environmental factors with heritability estimated at 0.52.[12]

This work was initiated to gain further insight on GGT as indicator of oxidative stress and to find out how the levels of GGT vary in non-alcoholic individuals as age progresses. The study also correlated the levels of GGT as the age increases in patients with essential hypertension and type 2 diabetic subjects.

MATERIAL AND METHODS

The study was conducted in the Department of Physiology, B.M.S.I., J.P.M.C, Karachi. The patients were recruited from outpatient department of Medicine J.P.M.C. Karachi. The study was carried out during the period of December 2006 to October 2007.

Grouping of Subjects:

The present study was cross-sectional study. The subjects were divided into three groups. Group (A) included 100 healthy normal subjects. Group (B) included 50 type 2 diabetic subjects with uncontrolled blood sugar levels. Group (C) included 50 patients with essential hypertension with raised blood pressure. Diabetes mellitus was defined according to the criteria set by the report on expert committee on the diagnosis and classification of diabetes.[13] Hypertension was defined according to the criteria set by JNC VII classification of hypertension.[14]

A stringent criterion was observed to include patients in the study. We excluded patients with acute or chronic liver, kidney and heart diseases, history of alcohol addiction, patients taking drugs affecting liver enzymes (carbamazepine, phenytoin, and barbiturates), patients suffering from cancer, persons using statins, females taking oral contraceptives and pregnant women. We also excluded subjects with hepatitis C virus antibody and heaptitis 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 the normal and subjects with total leukocyte count more than 10,000/µl.

A verbal informed consent of the patient were taken after explaining the procedure. All participants were asked to fast at least 12 hours and to avoid heavy physical activity for at least 2 hours before examination. After a 5 minute rest blood pressure was measured in sitting position.

All participants received a proforma, which included clinical examination having measure of; resting blood pressure, measure of height and weight, waist and hip circumference, daily physical activity, addiction of history of previous illnesses and types of medication.

Patient have venous blood (8 ml) was drawn from a disposable syringe. 2 ml was transferred to EDTA containing tube for complete blood count and remaining blood was clotted for collection of serum.

Complete blood count was performed by automated cell counter SYSMEX KX 21. Blood sugar was estimated by GOD-PAP Enzymatic Colorimetric Method. Hepatitis C virus antibodies are detected by chromatographic immunoassay (LG Quick card). Hepatitis B surface antigen is detected by qualitative immune-assay (Abbot Laboratory). Gamma GT was measured according to the Szasz method, standardised to IFCC.

Statistical Analysis

Analysis was carried out on SPSS version 14. Using one-way ANOVA, GGT levels were compared in the nor-mal, diabetic and hypertensive groups. All three groups were analysed by stratifying them into young, middle and elderly age groups. General characteristics were done using descriptive analysis. Pearson correlation was done with age and value of "r" was calculated in normal, diabetic and hypertensive subjects. Using Independent "t" test the general parameters were compared between normal and type 2

Table 1: *Comparison of Anthropometric measurement in hypertensive and controls.*

Anthropometric Measurements	Hypertensive (N = 50)	Controls (N = 100)	P-value
	Mean ± SEM	Mean ± SEM	
Height (meter)	1.67 ± 0.02	1.69 ± 0.01	0.279
Weight (kg)	71.2 ± 1.26	71.5 ± 0.66	0.793
BMI (kg/m²)	21.9 ± 0.26	21.1 ± 0.15	*0.019
Waist (cm)	91.89 ±1.56	83.82 ± 0.70	*0.001
Hip (cm)	80.52 ± 0.49	83.63 ± 1.14	0.350
Waist Hip ratio	1.13 ± 0.01	1.01 ± 0.01	*0.001

*P is significant at < 0.05 in comparison with control.

Table 2: *Comparison of Anthropometric measurement in diabetics and controls.*

Anthropometric measurements	Diabetics (N = 50)	Controls (N = 100)	P-value
	Mean ± SEM	Mean ± SEM	
Height (meter)	1.68 ± 0.02	1.69 ± 0.01	0.522
Weight (kg)	77.7 ± 1.54	71.5 ± 0.66	*0.001
BMI (kg/m²)	23.3 ± 0.42	21.1 ± 0.15	*0.001
Waist (cm)	92.35 ±1.44	83.82 ± 0.70	*0.001
Hip (cm)	83.87 ± 1.10	83.63 ± 1.14	0.092
Waist Hip ratio	1.12 ± 0.01	1.01 ± 0.01	*0.001

*P is significant at <0.05 in comparison with control.

Table 3: *GGT according to age in diabetics hypertensive and controls.*

Age (years)	G GT (IU/L)		
	Diabetics (N = 50)	Hypertensive (N = 50)	Controls (N = 100)
	Mean ± SEM	Mean ± SEM	Mean ± SEM
20 – 39	49.6 ± 3.60*	44.4 ± 1.51*	13.5 ± 0.61*
40 – 59	54.0 ± 1.34*	53.7 ± 1.39*	17.6 ± 0.69*
60 and above	63.9 ± 2.29 *	60.6 ± 3.56*	24.0 ± 1.18*
Gamma GT Vs Age	r= 0.41*	r = 0.61*	r = 0.76*

GGT significantly increases as age increases in all the three groups in vertical manner (*P <0.01).

Mean age, sex, waist hip ratio and BMI.

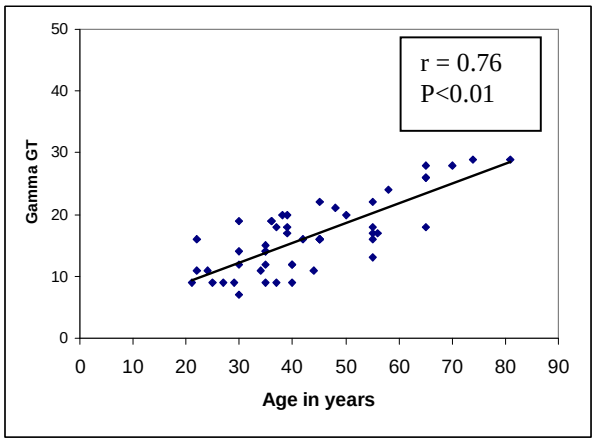

Fig. 1: *Correlation of gamma GT with age in controls.*

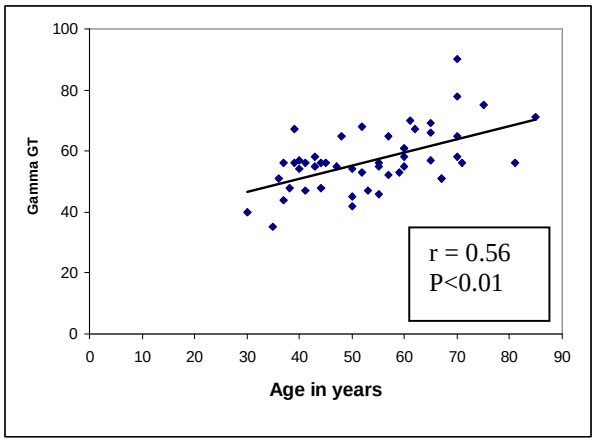

Fig. 2: *Correlation of gamma GT with age in diabetics.*

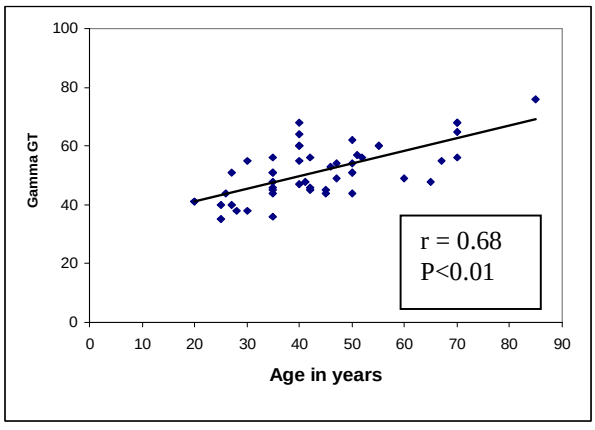

Fig. 3: *Correlation of gamma GT with age in hypertensive.*

diabetics and normal and hypertensive subjects.

RESULTS

Results were prepared on the basis of the following groups.

Comparison was made between normal, hypertensive and type 2 diabetics. In hypertensive individuals BMI, waist and waist hip ratio were significantly more than normal individuals, whereas in type 2 diabetics weight, BMI, waist and waist hip ratio were significantly higher than normal individuals (Table 1 and 2). High serum GGT levels were found to be positively associated with age in normal individuals, hypertensive and type 2 diabetics (Table 3). Age was found to be significantly related to increase in GGT in all the three groups in young, middle and elderly groups ($p < 0.01$). The value of "r" was found to be significant among all the three groups $p < 0.001$ (Table 3; Fig. 1, 2 and 3).

DISCUSSION

In the present study levels of Gamma glutamyltransferase were measured in normal persons and was compared with essential hypertension and type 2 diabetic patients who were life time nonalcoholic.

Pukka *et al.,* in their study showed that GGT levels rise with age in both sexes in abstainers and moderate alcoholics. He correlated GGT with age groups 18-30, 30-50, 50-70 and >70 years.[10] In comparison we excluded alcoholics and selected the age groups between 18-39, 40-59 and >60 years of age in both sexes. In their study GGT values were found to be increased as the age increases in all the three groups while Pukka *et al.,* in their study founded decreased levels of GGT in above 70 years of age.[10] This variation could be due to the selection of individuals, abstainers history of alcohol or number of subjects above 70 years of age, whereas previous studies have also reported increased GGT activities with increasing age[15-17] but they have mostly selected the abstainers rather than complete non alcoholics.

Studies on hypertensive and type 2 diabetics have also showed similar findings of increase in GGT values when compared with increase in age, waist hip ratio and BMI.[18-21] Our findings are in total agreement with these studies suggesting that this enzyme acts as an intervening factor in the association between obesity and diabetes and hypertension. It is known that GGT has a protective effect in maintaining appropriate hepatic glutathione levels, which are crucial in antioxidant defenses.[22] Therefore, it is possible that the generation of free radicals, which can occur in fatty liver and central obesity, may deplete intracellular glutathione and thus induce the activity of GGT into the circulation. This study clearly shows that some correla-

tion certainly exist between obesity and high GGT values. The study also indicated that as the age increased it is possible to get higher values of GGT. More studies are however needed to know the exact mechanism associated with this correlation. As GGT values varies widely among geographical boundaries associations, this study helps to identify role of GGT in normal persons as a stress marker and signify its importance with obesity in both hypertensive and diabetic individuals. Its role as a predictor for these two diseases needs further studies on large scale. As both hypertensive and type 2 diabetes mellitus are on the rise in Pakistan, it is need of the hour to perform the liver enzymes especially to find these associations on a large scale.

We, therefore, **conclude** the present study with the statement that GGT is an important marker of stress and increase as the age progresses independently without any association with alcohol. Its levels also have shown to be related with BMI and waist hip ratio in both hypertensives and type 2 diabetics suggesting its greater role in obesity.

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