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STUDY OF SERUM GGT LEVELS AND LIPID PROFILE IN DIABETIC PERIPHERAL NEUROPATHY

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ABSTRACT

Comparative study of gamma glutamyl transferase and lipid profile in diabetic patients with peripheral neuropathy and diabetic patients without any complications. Our study included 15 diabetic patients without any complications as control group and 30 diabetic patients with neuropathy as study group. Patients with history of alcoholism, acute and chronic illness were excluded from the study. The levels of GGT and HbA1C were significantly increased in study group when compared to control group. Even though levels of cholesterol, triglycerides LDL and VLDL are of not much significance, the atherogenic index ratio was calculated which was high in study group when compared to control group. Serum GGT can be used as an important marker in diagnosing diabetic peripheral neuropathy.

KEY WORDS: **Diabetic peripheral neuropathy, GGT, HbA1c levels, Type 2 DM.**

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INTRODUCTION

Diabetes mellitus in all its heterogeneity has taken the centre stage as one of the medical challenges and its complications are the major cause of morbidity and mortality in patients with DM. Diabetic patients are more prone to micro vascular complications namely diabetic neuropathy, nephropathy, retinopathy, which can impede their quality of life and macro vascular complications which increases morbidity and mortality (1). The prevalence of neuropathy is around 27.5% in type 2 DM patients (2). Diabetic peripheral neuropathy (DPN), a micro vascular complication of diabetes is the main predisposing factor for foot ulceration and infection characterized by pain, paresthesia and sensory loss. The pathophysiology of diabetic neuropathy includes several factors such as metabolic, vascular, immune, oxidative stress and neurohormonal growth factor deficiency (3). Recent studies have reported that oxidative stress may apparent in pathology associated with metabolic syndrome and neurodegenerative disease and suggested that serum gamma-glutamyl transferase may be an early marker of oxidative stress (4). GGT is a membrane bound enzyme which transfers glutamyl groups linked through the gamma carboxylic acid from peptides such as glutathione to acceptors. Its main physiological function is to make cysteine available for regeneration of intracellular glutathione and thereby protect against oxidative stress. Some of the recent studies have reported that oxidative stress may apparent in pathology associated with metabolic syndrome and neurodegenerative diseases suggesting that GGT may be an early marker of oxidative stress(5). Studies have shown that dyslipidemia is a significant contributor in the development of neuropathy via inducing oxidative stress in root ganglia sensory neurons (6). Therefore we investigated the relationship between diabetic peripheral neuropathy and serum GGT as a marker of oxidative stress.

MATERIAL AND METHODS

Biochemical evaluations include fasting glucose, postprandial glucose, HbA1c, GGT and Lipid profile. Blood samples were collected after an overnight fast of 12 hours and analyzed for plasma glucose, lipid profile; HbA1c and GGT were analyzed in auto analyzer Beckman Coulter by using enzymatic kit method.

INCLUSION CRITERIA

The study included 30 diabetic patients with peripheral neuropathy as study group and 15 diabetic patients without neuropathy as control group who were admitted in our SRM MC Hospital and research centre for treatment purpose.

EXCLUSION CRITERIA

Patients who had acute infections, liver diseases, alcoholics, neuropathy and retinopathy patients were excluded from the study. Informed consent were observed in the study. The study protocol was approved by ethical committee.

STATISTICAL ANALYSIS

All statistical data were analyzed by student's t – test to compare the significance between diabetic neuropathy and diabetic patients without neuropathy. Data were expressed as mean ± SD. P – Value of less than 0.05 ($P<0.05$) is considered as statistically significant.

RESULT

The results showed that there is an increased serum GGT level in study group when compared to control group. There is significant association between raised GGT levels and blood sugar levels. Increased levels of fasting

plasma sugar, postprandial blood sugar and HbA1c were found in our study indicating a poor glycemic control in study group which has led to the development of peripheral neuropathy. We could not find any significant correlation between GGT and lipid profile.

DISCUSSION

The study was done with the purpose to identify the effects of raised blood sugar levels on the liver enzymes especially GGT. In our study, we have compared GGT levels in relation to raised plasma sugar levels and lipid profile. Puka etal also found elevated levels of GGT in their studies where they compared GGT levels in type 2 DM with normal people as control groups (*The American Journal of Clinical Nutrition 2006*). Another study by Hochan cho etal found corresponding elevated levels of GGT in patients with diabetic peripheral neuropathy (66.1±51.6, p=0.000) compared to control (26.6±15.4) *Korean Diabetes J. 2010 April; 34(2): 111–118*. Neuropathy is a micro vascular complication enhanced by poor glycemic control and delayed by good glycemic control (12). Increased GGT levels are compared with lipid profile which includes TC, TGL, HDL, LDL, VLDL cholesterol. We could not find any significant correlation between GGT and lipid profile. Based on TGL, HDL and LDL levels atherogenic lipid ratio was calculated. Atherogenic index (TG – HDL)/HDL, LDL/HDL, log (TG/HDL) were significantly high in study group (4.44±1.5, p=0.001), (3.96±1.5, p=0.001) and (0.609±0.148, p=0.001) as compared to controls (2.65±1.11, 2.4±1.15, 0.382±0.177). Even though lipid profile was not of much significance there was marked increase of cholesterol, TGL, LDL and VLDL levels in study group when compared to controls. The levels of fasting blood sugar level, HbA1c and triglycerides were markedly increased among higher GGT categories. Our results suggested that the raised GGT levels are closely associated with the risk of diabetic complications as well as risk of atherosclerosis in patients with neuropathy when compared with controls. The toxic effects of hyperglycemia and its pathophysiologic derivatives such as oxidants, hyperosmolarity or glycation products can beexerted indirectly on tissues or by sustained alteration in cell signalling pathways (such as changes in phospholipids or kinases) induced by the products of glucose metabolism(11). Studies have shown that cellular GGT levels are closely related to oxidative stress indicators in vivo either as an antioxidant or prooxidant (8). Elevated GGT also indicates the subclinical inflammation (9). GGT plays a central role in the glutathione homeostasis by initiating the breakdown of extra cellular glutathione, which is an important antioxidant defense mechanism in cell. Increase in serum GGT activity indicates increase in oxidative stress, as more of glutathione is transported into the cells. This supports the role of GGT in inflammation and oxidative stress (10). The significance of high log (TG/HDL) ratio indicates the presence of small density LDL and may herald the existence of atherosclerosis. This data is insufficient to explore the hidden atherosclerosis and further studies will help in determining athero sclerosis.

CONCLUSION

Glycemic control is the central component of treatment. It is challenge for type II diabetic patients to maintain good glycemic control for the prevention of metabolic complication such as retinopathy, neuropathy, and nephropathy and cardio vascular complications. Glycemic control should be achieved by life style modifications and regular monitoring of blood glucose levels. Additional studies on glutathione, vitamin-C, super oxide dismutase may prove useful in preventing the neuropathy in diabetes patients.

Table 1

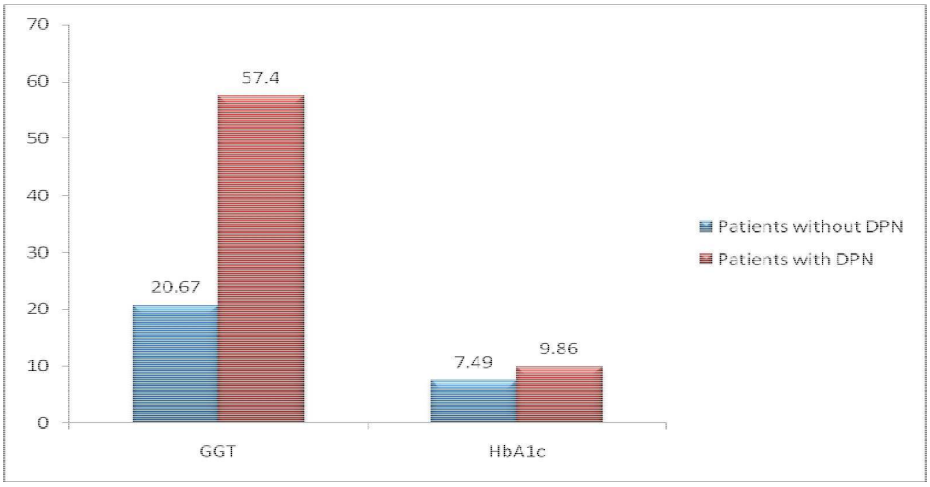
Comparison ***of serum fasting and postprandial blood sugar levels in patients with and without diabetic peripheral neuropathy (DPN).***

PARAMETERS	GROUPS	MEAN	STANDARD DEVIATION	P VALUE
	PATIENTS			
	WITHOUT	148.26	4.25	
FBS	DPN			
				0.001
	PATIENTS			
	WITH DPN	200.48	56.24	
	PATENTS			
	WITHOUT	215.80	75.19	
PPBS	DPN			0.002
	PATIENTS			
	WITH DPN	295.97	8.01	

Table 2

Comparison of serum GGT and HbA1c in patients with and without diabetic peripheral neuropathy (DPN)..

PARAMETERS	GROUPS	MEAN	STANDARD DEVIATION	P VALUE
	PATIENTS			
	WITHOUT	20.67	5.87	
GGT	DPN			
				0.001
	PATIENTS			
	WITH DPN	57.4	42.4	
	PATENTS			
	WITHOUT	7.49	0.72	
HbA1c	DPN			0.001
	PATIENTS			
	WITH DPN	9.86	1.65	



Biochemical parameters in control and study group

PAMETER	PATIENTS WITHOUT DPN (control)	PATIENTS WITH DPN (study group)	P - Value
Age	60.26±6.94	59.74±9.52	0.8
Duration	9.93±4.7	11.25±5.8	0.4
BMI	28.73±2.8	28.62±2.16	0.1
FBS	148.26±43.25	200.48±56.24	0.001**
PPBS	215.80±75.19	295.95±83.01	0.002
HbA1c	7.49±0.72	9.89±1.65	0.001**
GGT	20.60±5.87	57.4±42.4	0.001**
Cholesterol	147.13±26.74	178±48.39	0.006
TGL	130.93±54.74	137.97±42.04	0.661
HDL	42.33±15.48	35.05±10.67	0.112
LDL	98.93±40.77	114.42±44.50	0.241
VLDL	27.80±2.37	29.88±11.32	0.499
(TG-HDL)/HDL	2.65±1.11	4.44±1.35	0.001**
LDL/HDL	2.49±1.15	3.96±1.35	0.001**
Log TG/HDL	0.38±0.17	0.6±0.14	0.001**

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