



# The association between serum gamma glutamyltransferase levels and microalbuminuria in Type 2 diabetic patients

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## ABSTRACT

**Background and Objectives** Diabetic nephropathy is the major cause of chronic kidney disease and end stage renal disease in developing countries. Almost one third of the diabetic patients develop diabetic nephropathy in their life time. So it is pertinent to detect diabetic nephropathy at an early (microalbuminuric) stage. The aim of the study was to evaluate the association of serum GGT with microalbuminuria in type-2 diabetes mellitus.

**Methodology** The study comprised of 40 type-2 diabetes mellitus patients with normoalbuminuria and 40 type-2 diabetes mellitus patients with microalbuminuria categorised as Group I and Group II respectively.

**Results** In Pearson's correlation analysis of serum GGT with urine albumin levels, the correlation was not statistically significant in Group I subjects whereas in Group II, a statistically significant correlation was found. A statistically significant difference was observed between the mean values of fasting blood glucose, postprandial blood glucose, lipid profile, GGT, HbA1c between Group I and Group II.

**Conclusion** Interpretation of GGT levels may be a valuable parameter in the evaluation of microalbuminuria in Type 2 diabetes mellitus.

**Keywords:** *Microalbuminuria, Diabetic nephropathy, Gamma glutamyltransferase, Oxidative stress*

## INTRODUCTION

Diabetes mellitus is a serious public health problem because of its growing prevalence and chronic macro and microvascular complications ending up in an increase in mortality and morbidity<sup>1,2</sup>. In diabetic patients with proteinuria, the relative mortality is 40 times higher than in diabetic without proteinuria<sup>3</sup>.

Microalbuminuria is an important risk factor for progressive renal impairment. This holds true for diabetes mellitus patients and indicates who are likely to develop macrovascular disease and progressive renal impairment. Microalbuminuria arise from increased passage of albumin through filtration barrier.

Serum GGT is a nonprotein antioxidant of the cell present in serum, plasma membranes of all cells except erythrocytes, catalyses degradation of extracellular glutathione<sup>4,5,6</sup>. Serum gamma glutamyltransferase has commonly been used as a marker for excessive alcohol consumption and in liver disorder<sup>7,8,9,10</sup>. Emerging evidence suggest, GGT as a predictor of incident diabetes and Hypertension. Few studies have also shown that GGT predicts microalbuminuria and may also act as a predictor of microvascular complications in diabetes patients. Increased serum GGT activity observed in diabetic patients may be a response to oxidative stress that occurs during the course of the disease<sup>11,12,13</sup>. Accumulating data state that

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oxidative stress alters many functions of the endothelium leading to microalbuminuria.

There is paucity of data relating GGT and urinary albumin levels in type-2 diabetes mellitus patients. Therefore, a cross sectional study was performed to examine whether GGT, an oxidative stress marker is associated with microalbuminuria in diabetic patients.

#### MATERIALS AND METHODS

The study was conducted in Vinayaka Missions Kirupananda Variyar Medical College and Hospital, Salem, Tamilnadu, India, from January 2013 to August 2013.

This cross sectional study was carried out on type-2 diabetes mellitus patients with and without microalbuminuria who were categorized as Group II and Group I respectively. The number of study subjects were 80 totally, forty in group I and forty in group II. Study was approved by the institutional ethical committee and written informed consent was taken from all the patients.

#### INCLUSION CRITERIA

All the patients attending the Diabetic clinic diagnosed as per the American diabetic association criteria were considered for the study. Only those patients who were negative for albumin [macroalbuminuria] in urine by albustix method were taken.

#### EXCLUSION CRITERIA

Patients with Urinary tract infection, acute illness, congestive cardiac failure, patient on ACE inhibitor for hypertension and pregnant women were

excluded. Samples were not collected after exercise and immediately after surgery.

Biochemical parameters analysed for the study subjects were fasting blood glucose, postprandial blood glucose, HbA<sub>1c</sub>, GGT, total cholesterol, High density lipoprotein, Triglycerides, urea, creatinine and urinary albumin levels. Low density lipoprotein and Very low density lipoprotein were calculated using the Friedewald's formula.

Plasma Glucose and Serum Creatinine were estimated by GOD-POD method and Jaffe's reaction respectively. Serum triglycerides and serum cholesterol were analyzed by enzymatic, end point method. Direct enzymatic method and Berthelot method were used for analysing serum HDL and blood urea respectively. Urinary albumin was estimated by immunoturbidimetric method based on the following principle. Anti-human albumin antibodies react with the antigen human albumin in the sample to form antigen-antibody complexes which following agglutination is measured turbidimetrically. GGT was estimated by IFCC method. GGT catalyses the transfer of glutamic acid to acceptor glycyl glycine. This process releases 5 amino 2 nitrobenzoate, which is measured at 405nm.

#### STATISTICAL ANALYSIS

Statistical analysis was done by SPSS software. Data were given as mean  $\pm$  standard deviation. Correlation between the variables was assessed by Pearson's correlation coefficient.

#### RESULTS

The biochemical parameters of the study subjects in group I and group II are shown in **Table 1**.

**Table 1** Biochemical parameters in study subjects

Variables	Group I (Mean $\pm$ SD)	Group II (Mean $\pm$ SD)	Significance
FBG (mg/dl)	117.6 $\pm$ 38.64	189.3 $\pm$ 68.5	<0.001
PPBG (mg/dl)	162.8 $\pm$ 22.25	326.1 $\pm$ 66.99	<0.001
TC (mg/dl)	200.4 $\pm$ 53.19	252 $\pm$ 76.6	<0.001
TGL (mg/dl)	149.2 $\pm$ 33.87	177 $\pm$ 70.4	0.02678
HDL (mg/dl)	46.38 $\pm$ 4.53	39 $\pm$ 7.5	<0.001
LDL (mg/dl)	124.2 $\pm$ 50.6	178 $\pm$ 71	<0.001
HbA <sub>1c</sub> %	5.82 $\pm$ 0.78	8.04 $\pm$ 1.22	<0.001
Urea (mg/dl)	31.13 $\pm$ 6.68	33.55 $\pm$ 6.73	0.1097
Creatinine (mg/dl)	0.96 $\pm$ 0.24	1.05 $\pm$ 0.22	0.0771
Gamma GT (mg/dl)	20.65 $\pm$ 5.56	24.08 $\pm$ 5.0	0.00491
Microalbumin (mg/l)	18.95 $\pm$ 6.76	171.6 $\pm$ 85.77	<0.001



**Table 2** shows the Pearson correlation coefficient of serum GGT with urine albumin levels. In Group I, the correlation was not statistically significant. In group II patients, a statistically significant correlation was found between serum GGT with urinary albumin levels.

**Table 2 Correlation of GGT with Urine albumin levels**

	r Value	P Value
Group I	0.076	0.642
Group II	0.757	<0.0001

Elevated levels of GGT in type-2 diabetes mellitus patients with exclusion of other causes of GGT elevation might indicate microalbuminuria.

Mean values of group II is higher than group I except HDL which was lower indicating diabetic patients with microalbuminuria are at more risk for cardio, cerebrovascular and renal complication.

## DISCUSSION

Diabetes mellitus is now a common endocrine disorder in India. The worldwide prevalence of diabetes was approximately 2.8% in 2000 and is estimated to grow 4.4% by 2030. The incidence of renal complication in type-2 diabetes is very high and 5 to 15% end up in ESRD<sup>14</sup>. The incidence of renal complication in type-2 diabetes is increasing because type-2 diabetes with nephropathy and ESRD exceeds type-1 diabetes. Earlier diagnosis and timely intervention will help to prevent its complications. The earliest clinically detectable stage even in subclinical disease is when the patients excrete minor amounts of albumin in urine. (i.e. 30 – 300mg of albumin / day) . It has been proved that microalbuminuria is a strong predictor of diabetic nephropathy<sup>15,16</sup> and also an independent risk factor for cardiovascular disease. Duration of diabetes has significant contribution for the development of microalbuminuria by prolonged exposure to hyperglycemia induced advanced glycosylation end product accumulation. Microalbuminuria is an indicator of endothelial dysfunction<sup>17</sup>. Early detection and reversal of microalbuminuria indicates resolution of generalized endothelial dysfunction and successful reduction of overall cardiovascular risk<sup>18</sup>.

Several studies have suggested that oxidative stress also alters endothelial dysfunction. Oxidative stress in diabetic patients has also been implicated in the pathogenesis of diabetic nephropathy.

Serum GGT, a marker of oxidative stress plays a central role in glutathione homeostasis and is widely distributed in various cells. High levels of GGT are associated with insulin resistance<sup>19,20,21,22</sup> and also involved in the development of type-2 diabetes mellitus.

In the present study, even though the serum GGT levels were within the physiological range, a significant positive correlation was observed between urinary albumin levels and GGT in group 2 patients. In contrast, no correlation was seen between GGT and urinary albumin levels in group I patients.

Duk-Hee Lee et al have observed that small increases in serum GGT indicate a successful defence mechanism and might lead to less endothelial dysfunction and microalbuminuria<sup>23</sup> which is contradictory to our finding. In their study they have observed that large increase of serum GGT may indicate more oxidative stress leading to microalbuminuria insisting a different association between serum GGT levels and microalbuminuria.

Statistical evidence in the present study indicates there is a strong correlation between GGT and microalbuminuria, indicating high normal range of serum GGT predicts latent nephropathy in type-2 diabetes mellitus patients. Elevation of serum GGT may be due to oxidative stress leading to endothelial damage resulting in microalbuminuria. Thus, high normal range of serum GGT may be considered as a predictor of microalbuminuria. The results of this study are consistent with the growing evidence suggesting GGT as, not only a marker of oxidative stress but also a marker of microalbuminuria.

## Limitations

Large sample size may be required to confirm the results of the present study.

## CONCLUSION

Upper normal range of serum GGT might indicate the onset of microalbuminuria in type-2 diabetes mellitus. Type-2 diabetic patients should be



analysed for microalbuminuria as well as serum GGT levels at regular intervals to detect nephropathy and for the better control over cardiovascular complications.

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