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Research Article

The Association Between Serum Gamma Glutamyl Transferase and Diabetic Nephropathy in Patients with Type 2 Diabetes Mellitus; A Cross Sectional Study

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Abstract

INTRODUCTION: Diabetic nephropathy (DN) is one of the major micro vascular complications of diabetes. , and it develops in approximately 40% of patients with Type 2 diabetes mellitus. Serum gamma-glutamyltransferase (GGT) is a cell-surface enzyme which is commonly used as a biomarker of liver injury. The relationship between serum γ-glutamyltransferase (GGT) and renal dysfunction is inconclusive. In this study, we examined the relationship between serum GGT and diabetic nephropathy (DN) in patients diagnosed with type 2 diabetes mellitus.

METHODOLOGY: A total of 119 diabetic patients on an opd basis or admitted as inpatients are included in this study. Complete blood panel was analyzed. GGT., microalbuminuria, urea, creatinine and kidney size were recorded for each participant.

CONCLUSION: In our study, elevated GGT was independently associated with diabetic nephropathy in type 2 diabetes patients. Serum GGT is a good indicator for risk of diabetic nephropathy and can be used as a predictor of diabetic nephropathy.

Keywords: Diabetic nephropathy (DN) · γ-Glutamyltransferase (GGT) · Type 2 diabetes mellitus (T2DM) , Albumin

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Introduction:

Diabetes mellitus (DM) is a systemic disease characterized by micro vascular and macro vascular complications, and is becoming an increasing drawback worldwide [1]. Diabetic nephropathy (DN) is one of the major micro vascular complications of diabetes, and it develops in approximately 40% of patients with Type 2 diabetes mellitus [2]. Together with major cardiovascular risk and metabolic disorder, Diabetic nephropathy is becoming a serious issue to human health [1, 2,3]. Since few decades, the Mortality due to DN dramatically increased, which almost became one of the highest observed for all reported chronic diseases [2]. Meanwhile, as low early awareness of the disease in population and lack of effective therapies targeting DN when progressing to end stage renal disease (ESRD), it is imperative to urge further study for early identification and management of the risk factors to DN [2, 3]. There are various early predictive biomarkers of DN for early efficient identification of diabetic nephropathy. Microalbuminuria being a traditional marker of DN. , has recently been challenged for its weak correlation with renal

function and lacking sensitivity and specificity in early identification and evaluating DN [4–6]. However, there are many novel early predictive markers of DN developed in recent years, which are difficult to promote in clinical practice for their difficult accessibility and high cost [5–10].

Diabetic nephropathy is a leading cause of morbidity and mortality in diabetic patients (11). Diabetic nephropathy (DN) is typically defined by macro albuminuria (i.e. a urinary albumin excretion of more than 300 mg/day) or macro albuminuria and abnormal renal function as represented by an abnormality in serum creatinine or glomerular filtration rate (GFR) (12). Microalbuminuria is defined as persistent albumin excretion between 30 and 300 mg/day and, in patients with diabetes mellitus, may be indicative of early diabetic nephropathy, unless there is some coexistent renal disease (13).

Serum gamma-glutamyltransferase (GGT) is a cell-surface enzyme which is commonly used as a biomarker of liver injury. Serum GGT activity is widely used for the diagnosis of liver and obstructive biliary diseases and also as an indicator of alcohol consumption [14]. However, serum GGT is a sensitive but not very specific test in clinical laboratories, as there are other conditions that can also cause high serum GGT [14–16]. Many more studies have shown that serum GGT is proposed as an early and sensitive marker of oxidative stress and could be correlated with some disease or pathophysiological status like cancer, metabolic syndrome (MetS), atherosclerosis, and cardiovascular disease [15, 16].

Gamma-glutamyltransferase (GGT) is an enzyme located on the plasma membranes of several cells and tissues with a predominance of the liver (18). It has been reported that GGT might be an early and sensitive marker of oxidative stress even when within the normal range (19) and is related to a greater risk of hypertension, incident diabetes mellitus, CVD, CVD-associated mortality, and all-cause mortality as well as endothelial function in chronic kidney disease (20-23).

In this study, we aimed to investigate whether serum GGT levels were associated with microalbuminuria in patients with diabetes mellitus.

METHODS:

Sample size: sample size was estimated from huifang dai et al parent study by the formula -

$$n = \frac{Z_{\alpha/2}{}^2 * \sigma^2}{d^2}$$

Where:

n = The sample size

$Z_{\alpha/2}$ = The standard normal distribution, typically 1.96 for 95% CI

σ = The standard deviation.

d = The desired precision level (Expected variation from mean)

Using the above values at 95% Confidence level a sample size of 100 subjects will be included in the study.

Considering 10% Nonresponse a sample size of 100 + 10 = 110 subjects will be included in the study.

Inclusion criteria:

- Patients willing to give written informed consent
- Patients with type 2 diabetes mellitus

Exclusion criteria

- Age <18 yrs.
- Active or chronic inflammation
- Autoimmune diseases
- Malignancy
- Acute or chronic renal/hepatic diseases, or coronary artery disease
- Type 1 diabetes
- Alcohol consumption≥20 g/ day in the last 3 month
- Previous diagnosis of acute or chronic liver disease
- Intake of hepatotoxic drugs
- Inflammatory diseases

Statistical Analysis

All the data will be compiled in Microsoft excel and Descriptive statistics will be calculated. To compare the quantitative variables t-test or Mann-Whitney U test will be used. To compare the qualitative attributes Chi-square test or Fisher's exact test will be used. To find the correlation between variables Karl Pearson correlation coefficient or spearman's rank correlation will be used. The data will be analyzed using statistical software.

Methodology

Diabetic patients on an opd basis or admitted as inpatients are included in this study. Information is collected and detailed history is taken using pre-formed proforma (Annexure 2) at the time of admission. The diagnosis of T2DM was made according to the American Diabetes Association guidelines. Complete renal examination was applied to all participants, the diagnosis of nephropathy was made by microalbuminuria, kidney size. Venous blood samples were taken after an overnight fast. All biochemical analyses were studied which include microalbuminuria, renal function tests, GGT.

Complete blood panel was analyzed GGT, microalbuminuria, urea, creatinine and kidney size were recorded for each participant.

Results :

Demographic profile:

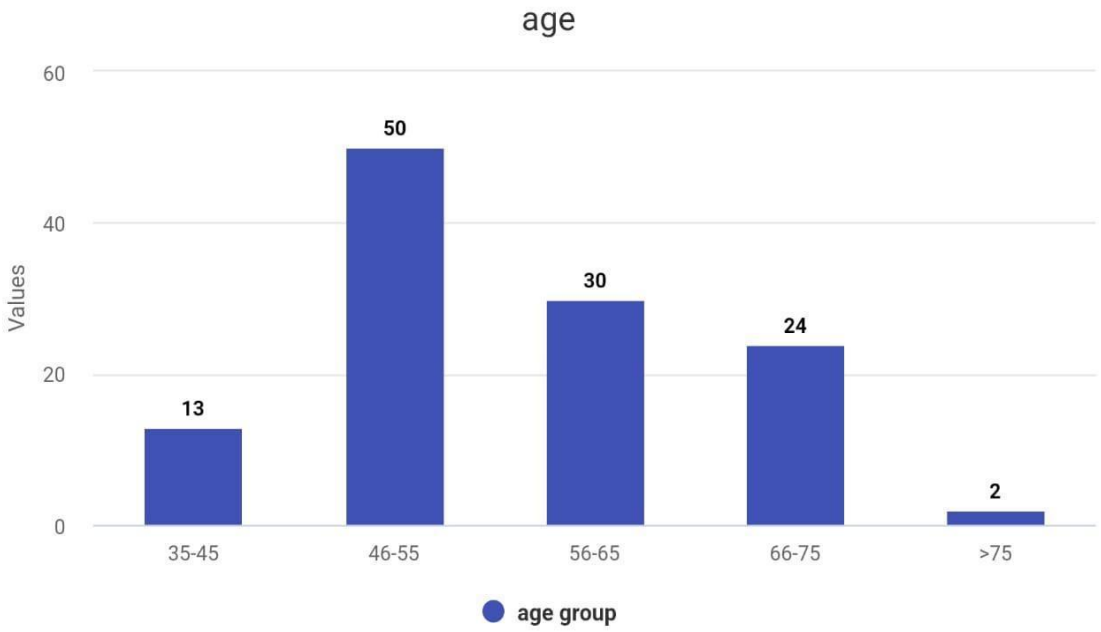

Figure 1- Age distribution

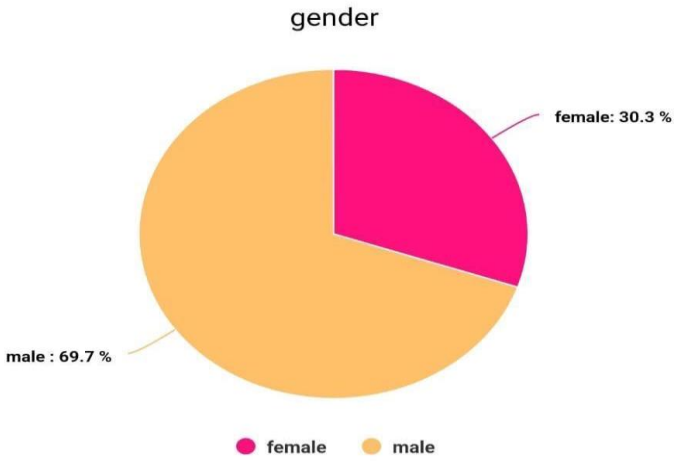

Figure 2- sex distribution

Among 119 patients, the mean age is 56.65. Maximum age of >75 years and minimum of age 35 years. **Figure 1**. 83(69.7%) were male and 36(30.3%) were female. **Figure 2**.

Table 1; BASIC CHARACTERISTICS

VARIABLES	VALUES
sample size	119
age, mean (SD)	56.65 (9.67)
gender	Female - 36, Male - 83
duration of diabetes(years), mean(SD)	8.84(5.81)
HB1ac, mean(SD)	8.89(2.65)
FBS, mean (SD)	179.44(96.35)
PPBS, mean(SD)	252.07(136.59)

In our study, mean duration of diabetes is 8.84 +/- 5.81, mean HBA1c is 8.89 +/- 2.62.
Mean FBS and PPBS were 179.4 +/- 96.3 and 252 +/- 136.5 respectively (table 1).

Table 2; Correlation of patients with diabetic nephropathy and diabetic patients without nephropathy

Variables	Type 2 DM with nephropathy	Type 2 DM without nephropathy	p value
Albumin(mean)	0.695	1.923	0.035
total protein,mean(SD)	6.58(0.86)	6.75(1.35)	0.51
ALT,median (IQR)	17 (12, 32)	18.35(12, 28)	0.92
AST median(IQR)	19 (14, 30)	19.05 (12.5, 30)	0.84
TLC median(IQR)	8540 (7880, 9970)	7615 (6080, 9560)	0.023
platelet, median (IQR)	2.68 (1.94, 3.12)	2.62(1.98, 3.25)	0.81
Creatinine, median (IQR)	1.6 (1.2, 2.4)	0.7(0.6, 1.1)	<0.001
urine PCR, median (IQR)	0.5(0.38, 0.8)	0.4(0.27, 0.55)	0.014
GGT, median (IQR)	65(36, 120.5)	37(19.1, 66)	0.002

- Mean albumin among diabetic nephropathy patients is 0.69 and in diabetic patients without nephropathy is 1.92. This difference is statistically significant with p value of <0.05.

Mean total protein among diabetic nephropathy patients is 6.58 and in diabetic patients without nephropathy is 6.75

- Median(IQR) ALT among diabetic nephropathy patients is 17 (14-30) and in diabetic patients without nephropathy is 19.05 (12.5-30). This difference is statistically not significant with p value of 0.84.
- Median(IQR) total leukocyte count among diabetic nephropathy patients is 8,540 (7880-9970) and in diabetic patients without nephropathy is 7,615 (6080-9560). This difference is statistically significant with p value of <0.05.
- Median(IQR) creatinine among diabetic nephropathy patients is 1.6(1.2-2.4) and in diabetic patients without nephropathy is 0.7 (0.6-1.1). This difference is statistically significant with p value of <0.05.
- In our study, median(IQR) GGT in diabetic nephropathy is 65(36-120.5) and median(IQR) GGT in diabetic patients without nephropathy is 37(19.1-66). This difference is statistically significant with p value <0.05(table 2).

DISCUSSION

Diabetic nephropathy (DN) is one of the major micro vascular complications of diabetes , and it develops in approximately 40% of patients with Type 2 diabetes mellitus.Together with major cardiovascular risk and metabolic disorder, Diabetic nephropathy is becoming a serious issue to human health. In a few decades, the Mortality due to DN dramatically increased, which almost became one of the highest observed for all reported chronic diseases [2].

Serum gamma-glutamyltransferase (GGT) is a cell-surface enzyme which is commonly used as a biomarker of liver injury. Serum GGT activity is widely used for the diagnosis of liver and obstructive biliary diseases and also as an indicator of alcohol consumption [14].

In our study, the sample size is 119 , out of which 83 are males and 36 are females.

In our study, mean albumin among diabetic nephropathy patients is 0.695 and which is statistically significant with p value <0.05. In Junlin Zhang et al.[24] Hypoalbuminemia was associated with poor renal prognosis in patient with diabetic nephropathy.

Total leukocyte count among diabetic nephropathy patients was significantly with p value (0.05). In sedigheh Moradi et al.[25] , an elevated total leukocyte count was associated with chronic complications of type 2 diabetes mellitus. In Chirag LU et al.[26] and Devamsh GN et al.[26], an elevated neutrophil and neutrophil lymphocyte ratio was associated increased risk of diabetic nephropathy.

Increased Serum GGT is associated with diabetic nephropathy with significant p value (<0.05).In Kan Sun et al.,[28] increased serum GGT level is independently associated with prevalence of albuminuria in a large population- based cohort. In Huifang Dai et al.,[29] there was an independently positive relationship between serum GGT levels and DN, which suggested that elevated GGT was a potential indicator for risk of DN. In Aydin Unal et al.,[30] Serum GGT levels were significantly higher in microalbuminuric diabetic patients.

LIMITATION :

- single center study
- Small group of population.

CONCLUSION:

In our study, elevated GGT was independently associated with diabetic nephropathy in type 2 diabetes patients.

Serum GGT is a good indicator for risk of diabetic nephropathy and can be used as a predictor of diabetic nephropathy.

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Author's Contribution:

AHR- Definition of intellectual content, Literature survey, Prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation andsubmission of article; MTR- Concept, design, clinical protocol, manuscript preparation, editing, manuscript revision, Design of study, statistical Analysis and Interpretation; MS- Review Manuscript, Literature survey and preparation of Figures; AAG- Coordination and Manuscript revision

Conflict of interest: No! Conflict of interest is found elsewhere considering this work.

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