ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
Index Copernicus Value: 68 . 16
PubMed - National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 5, Issue –3, May - 2020, Page No. : 97 - 103

To study the correlation of Serum GGT levels in patient with diabetic Nephropathy in patients with diabetes mellitus type II.

[1]Dr. Dharmendra Kumar Verma, J L N Medical College, Ajmer

[2]Dr. Ravi Kumar Bansal, Senior Resident J L N Medical College, Ajmer

[3]Dr. Vikas Kumar Agarwal, Senior Resident SK Govt Medical College, Sikar

Corresponding Author: Dr. Ravi Kumar Bansal, Senior Resident J L N Medical College, Ajmer

Citation this Article: Dr. Dharmendra Kumar Verma, Dr. Ravi Kumar Bansal, Dr. Vikas Kumar Agarwal, "To study the correlation of Serum GGT levels in patient with diabetic Nephropathy in patients with diabetes mellitus type II", IJMSIR- May - 2020, Vol – 5, Issue -3, P. No. 97 – 103

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Introduction: Diabetes Mellitus is a complex disease characterized by chronic hyperglycemia with various long term complications. Serum GGT is considered as indicators of oxidative stress and is well known for it's predictive value in diabetic microvascular complications. Aim of the present study was to evaluate the relationship between Serum GGT levels and microvascular complications i.e. diabetic Nephropathy.

Materials and Methods: The study included 100 patients (test group) & 100 control group. In this study, serum GGT, FBS, PP2hr, HBA1c, RFT & Urine ACR was done. Data was tabulated and analyzed using appropriate tests.

Observations And Results: In this study , serum GGT levels of 100 clinically established type-2 diabetics cases and 100 healthy controls (both of above 35 years) were compared. Mean Serum GGT levels in case group with microvascular complications & without complications was 51.99 ± 9.66 & 40.3 ± 15.99.

Conclusion: In this study, there was a significant difference in Serum GGT levels of cases & control. Hence serum GGT levels can be used as an early, cheap and alternative predictive marker of diabetic microvascular complications viz. diabetic Nephropathy.

Keywords: Diabetes, Serum GGT, Urine ACR .

Introduction

Diabetes mellitus: Diabetes is a Group of metabolic diseases characterized by hyperglycaemia resulting from defect in insulin secretion, insulin action or both. It is single most important disease which can affect nearly every organ system in the body[1].

India has the world's second largest population living with diabetes. In 2013, there were 65.1 million people between 20 and 79 years of age with diabetes and this number is predicted to rise to 109 million by 2035[2].

It is characterised by chronic hyperglycaemia, metabolic abnormalities and long-term macro vascular and micro vascular complications involving the blood vessels, eyes, kidneys and nerves.

Diabetic nephropathy: It 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.

GGT: Gamma-Glut amyl transferase E.C.2.3.2.2, (5-L-Glutamyl)-peptide:amino-acid 5-glutamyl transferase. (gamma-glutamyl transpeptidase E.C.no-2.3.2.2) is a microsomal enzyme which has 11-isoenzyme. It is seen in liver, kidney, pancreas, intestinal cells and prostate gland. It is elaborated by extra hepatic tissues including kidney epididymis, fibroblasts, lymphocytes and lung. Its normal value in serum is 7-35 U/L in female and 10-50U/L in male. Its level is highly elevated in alcoholism, obstructive jaundice, neoplasm, diabetes and inflammation. The highest activity was in the kidneys, where GGT was localized to the luminal surface of the proximal tubule cells (Duk-Hee Lee, 2005)[3].

Study Design: Cross sectional study

Sample

- The study was conducted in Department of General Medicine, J.L.N Medical College and Associated Group of Hospitals, Ajmer.
- The study included 100 patients (test group) & 100 control group.
- After admission, thorough clinical examination was carried out and relevant investigations were performed.

Inclusion Criteria

- Patients with diabetes mellitus Type II on oral hypoglycaemic agents and/or Insulin therapy.
- Age more than 35years.

Exclusion Criteria

Following patients were excluded from the study

- Age <35yrs
- Patients with other co-morbidities like chronic liver disease, chronic lung disease, chronic kidney disease, malignancies
- Chronic alcoholics.
- Patients on ACE Inhibitor/ ARB therapy and other nephrotoxic drugs.

Methodology

After informed consent from the enrolled patients, a questionnaire was prepared to obtain details of the patient's address, sex, age, occupation and symptoms if any. History of diabetes, its duration, drug history and potential complications was given special importance. The patient's vitals and parameters were recorded.

A. Routine laboratory investigations:

a. Complete blood picture auto analyzer method
b. RFT-blood urea and serum creatinine, LFT
c. Urine R/M: By auto analyser
d. Blood sugar (fasting, post-prandial) –glucose oxidase-peroxidase methods
e. HbA1c-high performance liquid chromatography is D-10 auto analyser

B. Special Investigations

1. **Serum GGT :** CARBOXY SUBSTRATE METHOD
2. Urinary Albumin-creatinine ratio

Diabetic Nephropathy: Among the clinically important manifestations of secondary microvascular complications of diabetes, kidney as a target organ represents a health problem of enormous social cost[4]. Diabetic nephropathy is a devastating complication of diabetes mellitus and is among the leading indications for dialysis and kidney transplantation.

Natural history of diabetic nephropathy is duration dependant and extends over many years before clinical expression becomes evident. It is a multistage condition that requires several years to become clinically overt. The stages are (i) incipient nephropathy (ii) overt nephropathy (iii) advanced nephropathy and (iv) end stage renal disease[5].

Microalbuminuria & urinary albumin: creatinine ratio (ACR)

Microalbuminuria is defined by a rise in urinary albumin loss to between 30 and 300mg day. Timed urine collections may be inaccurate and therefore a **urinary albumin: creatinine ratio (ACR)** >2.5 mg/mmol in men and >3.5mg/mmol in women is often used to define microalbuminuria. This is the earliest sign of diabetic kidney disease and predicts increased total mortality,

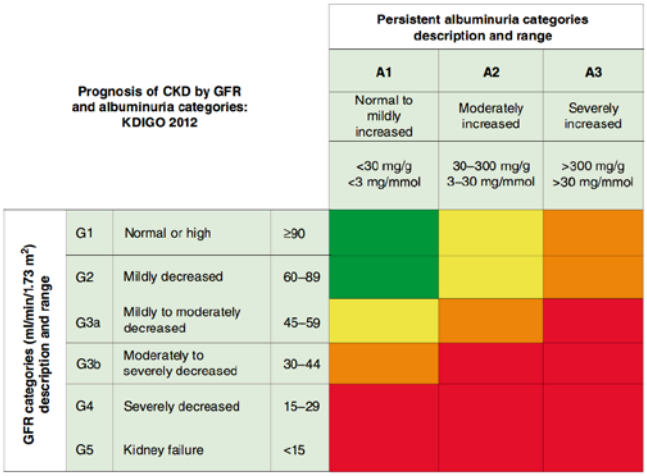
Table 1: Stages of classic diabetic nephropathy according to urinary albumin level 1 Stage of nephropathy

	Urine dipstick for protein	Urine ACR (mg/mmol)	24-urine collection for albumin* (mg/day)
Normal	Negative	< 2.0 (men) < 2.8 (women)	<30
Microalbuminuria	Negative	2. 0 – 20.0 (men) 2.8 – 28.0 (women)	30-300
Overt nephropathy (Macroalbuminuria)	Positive	> 20.0 (men) > 28.0 (women)	>300

According to the KDOQI guidelines of the NKF, CKD will be stratified into the following stages based on eGFR:

- Stage 1: GFR ≥ 90 and Albumin excretion rate (AER) > 30mg per 24 hr.
- Stage 2: GFR 60-89 and AER >30mg per 24 hr.
- Stage 3: GFR 30-59.
- Stage 4: GFR 15-29.
- Stage 5: GFR < 15.

(All values of GFR are in ml/min/1.73m2 BSA)



Kidney Disease I m proving Global Outcome (KDIGO) classification of chronic kidney disease (CKD). Gradation of color from green to red corresponds to increasing risk and progression of CKD, GFR, glomerular filtration rate.

Statistical analysis

The data was coded and entered into Microsoft Excel spreadsheet. Analysis was done using SPSS version 20 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) Windows software program. Descriptive statistics included computation of percentages, means and standard deviations. The independent t test (for quantitative data within two groups) was used for quantitative data comparison of all clinical indicators. Chi-square test used for qualitative data whenever two or more than two groups were used to compare. Level of significance was set at $P \leq 0.05$.

Table 2: Age Wise Comparison of Groups

	N	Mean	S.D.	Min.	Max.	P value
Case	100	58.02	10.53	35.00	83.00	0.66
Control	100	57.35	11.55	35.00	83.00	
Total	200	57.68	11.03	35.00	83.00	

T test=1.56, df=198

Case (58.02) showed slightly more aged patients as compared to control (57.35) which showed statistically non-significant results.

Table 3: Gender Wise Comparison of Groups

		Case		Control	
		N	%	N	%
Gender	M	63	63	41	41
	F	37	37	59	59
Total		100	100	100	100

X^2 test=1.22, df=1, P value=0.83

Male patients registered higher in the study as compared to female.

Table 4: Blood Sugar Wise Comparison of Groups

		N	Mean	S.D.	Min.	Max.	T / df	P value
FBS	Case	100	160.95	30.62	128.00	279.00	20.02 / 198	0.001(S)
	Control	100	97.35	8.43	75.00	110.00		
	Total	200	129.15	38.96	75.00	279.00		
PPBS	Case	100	242.05	38.106	185.00	375.00	8.29 / 198	0.001(S)
	Control	100	124.42	21.18	17.00	148.00		
	Total	200	183.23	66.5002	17.00	375.00		

Case showed more mean score of FBS and PPBS as compared to control which showed statistically significant results.

Table 5: Blood Reports Wise Comparison Of Groups

		N	Mean	S.D.	Min.	Max.	T / df	P value
Blood urea	Case	100	41.59	9.38	7.50	64.60	5.69 / 198	0.001 (S)
	Control	100	34.93	6.98	18.30	48.30		
	Total	200	38.26	8.89	7.50	64.60		
Serum creatinine	Case	100	1.12	0.35	0.11	2.10	7.63 / 198	0.001 (S)
	Control	100	0.807	0.22	0.34	1.30		
	Total	200	0.96	0.33	0.11	2.10		
HBA1C	Case	100	8.77	1.33	6.20	11.50	30.72 / 198	0.001 (S)
	Control	100	5.88	0.51	4.80	5.90		
	Total	200	6.83	2.19	3.80	11.50		
SGGT	Case	100	51.99	9.66	31.00	78.00	8.55 / 198	0.001 (S)
	Control	100	40.3	15.99	15.00	87.00		
	Total	200	46.14	14.42	15.00	87.00		
UACR	Case	100	75.62	83.0	12.00	376.00	9.704 / 198	0.001 (S)
	Control	100	22.1	7.37	7.00	64.00		
	Total	200	48.86	64.60	7.00	376.00		

Case showed more mean score of blood urea, serum creatinine, HBA_1C, SSGT and UACR compared to control which showed statistically significant results.

Graph 1: Blood Reports Wise Comparison Of Groups

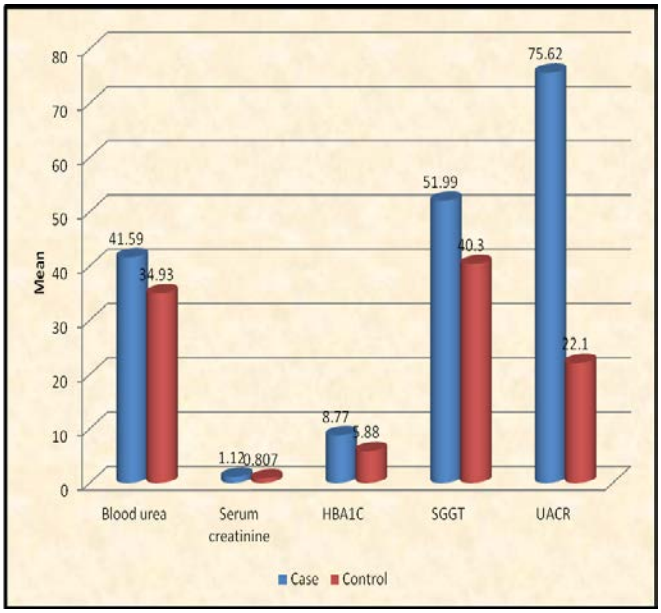
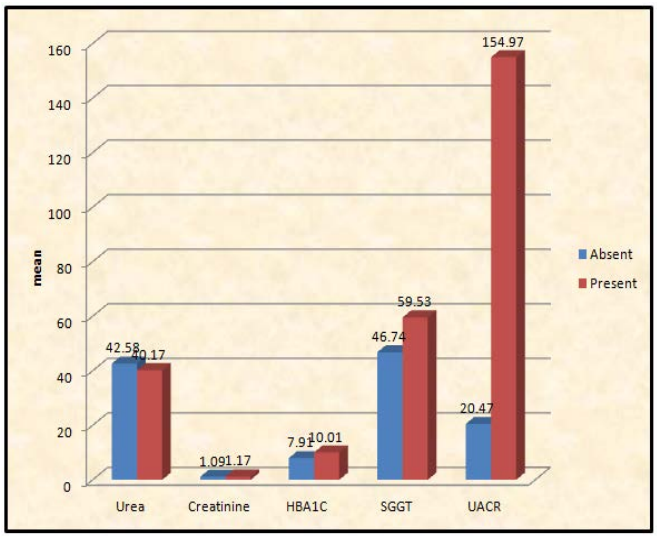


Table 6: Comparison of Study Variables among Diabetes Nephropathy [N=100 (Cases)]

		N	Mean	S.D.	Mean differences	T / df	P value
Urea	Absent	59	42.58	9.11	2.406	1.91/198	0.209
	Present	41	40.17	9.68			
Creatinine	Absent	59	1.09	0.33	0.07	-0.096 / 198	0.27
	Present	41	1.17	0.38			
HBA1C	Absent	59	7.91	0.86	2.09	-2.79/198	0.001 (S)
	Present	41	10.01	0.809			
SGGT	Absent	59	46.74	7.15	12.79	0.05/198	0.001 (S)
	Present	41	59.53	7.61			
UACR	Absent	59	20.47	3.64	134.501	-5.86/198	0.001 (S)
	Present	41	154.97	78.04			

In Case group (total=100), mean score of serum creatinine, HBA_1C, SSGT and UACR were higher in diabetes nephropathy as compared to without diabetes nephropathy which showed statistically significant results.

Graph 2: Comparison of Study Variables among Diabetes Nephropathy [N=100 (Cases)]



Discussion

The present study reports a case control study on the predictive value of ϒ-GT for microalbuminuria in type 2 diabetics. Renal disease (Diabetic nephropathy) is a common complication of type 2 diabetics. Prevalence of DN is very high and 5 - 15% enters the stage of ESRD. (Safdar et al[6] 2015). Earlier most stage of DN is called incipient DN which may be subclinical when it can be detected by minor urinary albumin amounts of 30 – 300mg/day). (Viswanathan et al[7]2012).

Microalbuminuria is a strong predictor of DN and an independent risk for the coronary artery disease. (Chadban et al[8]. 2010; Chowta et al[9] 2009) Microalbuminuria has association with the duration of type 2 DM. Chronic hyperglycemia contributes to the advanced glycosylation end product (AGE) which causes endothelial dysfunction and albuminuria ensues. (Manjrekar et al[10] 2010).

If microalbuminuria is detected earlier, then timely intervention may prove helpful in dampening the

generalized endothelial dysfunction. (Satchell et al[11] 2008) Chronic hyperglycemia increases oxidative stress to the vascular endothelium. (Şarlı et al. 2013[12]; Onal et al[13] 2014; André et al[14] 2007) Vascular endothelium dysfunction of kidneys is the primary lesion of DN which is aggravated by oxidative stress too. The ϒ-GT plays role in the anti oxidative stress mechanisms through glutathione homeostasis. ϒ-GT is found nearly all of body cells. Previous studies reported positive association of ϒ-GT with insulin resistance in type 2 diabetics. (Zoppini et al[15] 2009; Grundy et al[16] 2007; Sabanayagam et al[17] 2009).

In the present study, the ϒ-GT was significant high range in cases (P=0.001) and showed positive correlation with microalbuminura. The ϒ-GT predicted the microalbuminuria significantly.

The finding of ϒ-GT is consistent with previous studies (Vijayasamundeeswari al[18] 2014; Nunes et al[19] 2012) which reported similar observations.

Evidence based finding of ϒ-GT of present study is worth finding, indicating high normal range of serum ϒ-GT may be used for predicting the incipient DN in type 2 diabetics. Raised serum ϒ-GT in type 2 diabetics may be exploited as a screening test for early detection of microalbuminuria and DN and then preventive measures may be taken at the earliest to prevent ESRD. The observations of present study are in agreement with previous studies. (Zoppini et al. 2009[103]; Grundy 2007[104]; Sabanayagam et al. 2009[105]; Lee et al. 2005) The ϒ-GT, even within high normal range, may be used for predicting the microalbuminuria.

Conclusion

The present study has shown that oxidative stress and serum GGT are some of the factors associated with diabetic micro vascular complications. Poor glycemic control as reflected by increased HbA1c causes worsening of micro vascular complications. Serum GGT is a useful marker for studying oxidative stress. It can be used as a surrogate marker of microvascular complications in diabetes mellitus. ϒ-GT levels along with urinary albumin should be routinely performed at regular intervals for earlier detection of diabetic micro vascular complication.

References

1. Pradeepa R, Deepa R, Mohan V Epidemiology of diabetes in India-current perspective and future projections. J Indian Med Assoc. 2002 Mar; 100(3):144-8.
2. Fauci AS, Braunwald E, Kasper DL, Mauser DL, Longo DL, Jameson JL, et al, editors, Harrison's Principles of internal medicine, diabetic retinopath, 19th ed. New York: McGraw Hill; 2422-2424.
3. Lee, Duk-Hee, David R Jacobs, Myron Gross and Michael Steffes. 2005. "Serum γ-Glutamyltransferase Was Differently Associated with Microalbuminuria by Status of Hypertension or Diabetes: The Coronary Artery Risk Development in Young Adults (CARDIA) Study." Clinical Chemistry, 51(7): 1185–91.
4. Arrigo Schieppati,1 Giuseppe Remuzzi, https://doi.org/10.1111/j.1523-1755.2005.
5. Giuseppe Pugliese, Acta Diabetol DOI 10.1007/s00592-014-0650-7
6. Safdar, Muhammad, and Syed Nayer Mahmud. 2015. "Frequency of Restless Leg Syndrome in End Stage Renal Disease Patients Undergoing Hemodialysis and Its Association with Diabetes Mellitus." Rawal Medical Journal, 40(3): 273–76.
7. Viswanathan, Vijay, Priyanka Tilak, and Satyavani Kumpatla. 2012. "Risk Factors Associated with the Development of Overt Nephropathy in Type 2 Diabetes Patients: A 12 Years Observational

Study." The Indian Journal of Medical Research, 136(1): 46.

8. Chadban, S, M Howell, S Twigg, M Thomas, G Jerums, A Cass, D Campbell, K Nicholls, A Tong, and G Mangos. 2010. "Assessment of Kidney Function in Type 2 Diabetes." Nephrology, 15(s1): S146–61.
9. Chowta, NK, P Pant and MN Chowta. 2009. "Microalbuminuria in Diabetes Mellitus: Association with Age, Sex, Weight and Creatinine Clearance." Indian Journal of Nephrology, 19(2): 53.
10. Manjrekar Poornima, A, R Shenoy and A Hegde. 2010. "Laboratory Assessment of the Diabetes Scenario with Respect to HbA1c and Microalbuminuria." Journal of Clinical and Diagnostic Research, 4: 2489–94.
11. Satchell, SC and JE Tooke. 2008. "What Is the Mechanism of Microalbuminuria in Diabetes: A Role for the Glomerular Endothelium?" Diabetologia, 51(5): 714–25.
12. Şarlı, Bahadır, Hüseyin Arınç, Ahmet O Baktır, Hayrettin Sağlam, Erkan Demirci, Yasemin Doğan, Serkan Kurtul, Abdulsamet Erden and Ahmet Karaman. 2013. "Serum Gamma Glutamyl Transferase and Alanine Transaminase Levels Predict Endothelial Dysfunction in Patients with Non-Alcoholıc Steatohepatitis." Journal of the American College of Cardiology, 62(18_S2): C81–82.
13. Onal, Ibrahim Koral. 2014. "Endothelial Dysfunction in Patients with Non-Alcoholic Steatohepatitis." Upsala Journal of Medical Sciences, 119(3): 290–91.
14. André, Philippe, Beverley Balkau, Marie Aline Charles and Eveline Eschwège. 2007. "γ-Glutamyltransferase Activity and Development of the Metabolic Syndrome (International Diabetes Federation Definition) in Middle-Aged Men and Women Data From the Epidemiological Study on the Insulin Resistance Syndrome (DESIR) Cohort." Diabetes Care. 30(9): 2355–61.
15. Zoppini, Giacomo, Giovanni Targher, Maddalena Trombetta, Giuseppe Lippi and Michele Muggeo. 2009. "Relationship of Serum γ-Glutamyltransferase to Atherogenic Dyslipidemia and Glycemic Control in Type 2 Diabetes." Obesity, 17(2): 370–74.
16. Grundy, Scott M. 2007. "Gamma-Glutamyl Transferase Another Biomarker for Metabolic Syndrome and Cardiovascular Risk." Arteriosclerosis, Thrombosis and Vascular Biology, 27(1): 4–7
17. Sabanayagam, Charumathi, Anoop Shankar, Jialiang Li, Cecil Pollard and Alan Ducatman. 2009. "Serum Gamma-Glutamyl Transferase Level and Diabetes Mellitus among US Adults." European Journal of Epidemiology, 24(7): 369–73.
18. Vijayasamundeeswari, CK and R Sudha. n.d. "The Association between Serum Gamma Glutamyltransferase Levels and Microalbuminuria in Type 2 Diabetic Patients."
19. Nunes, Luciana Macatrão Nogueira, Thiago Moreira de Olinda, Marta Maria de França Fonteles, Miguel Nasser Hissa, Silvânia Maria Mendes de Vasconcelos, Daniel Freire de Sousa and Maria Goretti Rodrigues de Queiroz. 2012. "Monitoring Biochemical Markers during Pharmacotherapeutic Follow-up of Type 2 Diabetic Patients." Revista de Ciências Farmacêuticas Básica E Aplicada, 33(3): 409–14.