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Original article:

Study of correlation of serum GGT levels in patient with diabetic retinopathy in patients with diabetes mellitus type II

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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 retinopathy.

Materials and methods-The study included 100 patients (test group) & 100 control group. In this study, serum GGT, FBS, PP2hr, HBA1c & fundoscopy 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 58.80 ± 7.77 & 48.32 ± 8.57.

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 retinopathy.

INTRODUCTION

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].Due to its very large population, 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 retinopathy is one of the most common and potentially devastating complications of diabetes mellitus. The onset of diabetic retinopathy one of the earliest micro vascular complication and also an indication for a more aggressive approach towards achieving normoglycaemia to prevent further complications.

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. 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 et al[3] 2005).

It can transfer gamma-glutamyl residues to substrate. It has a central role in the maintenance of intra cellular antioxidant defences through its mediation of extra cellular glutathione transport into most types of cells. Numerous studies have found that GGT is not just a marker of alcohol consumption, but is an independent predictor of many diseases, including cardiovascular diseases, type 2 diabetes, inflammation and possibly underlying oxidative stress (Emdin, Passino, et al[4], 2002; Emdin, Pompella, et al[5] 2005; Bo S et al[6]., 2005; Whitfield et al[7] 2001; Yamada et al[8]., 2006; Meisinger et al[9] 2005; Wannamethee et al.2005[10]; Sakuta, Suzuki, et al[11] 2005). Meisinger et al[12]. (2005) postulated that possible mechanisms by which GGT is a marker for increased risk of type 2 diabetes include 1) elevated serum GGT could indicate excess fat deposits in the liver, which may cause hepatic insulin resistance and increase the risk of type 2 diabetes by contributing to systemic insulin resistance; 2) increased GGT is a marker for oxidative stress or increased GGT may be the expression of inflammation.

MATERIAL AND METHODS:

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

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

EXCLUSION CRITERIA

Following patients were excluded from the study

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

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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:

1. Complete blood picture auto analyzer method
2. Blood sugar (fasting, post-prandial) –glucose oxidase-peroxidase methods & other LFT, RFT, LIPID PROFILE.
3. HbA1c-high performance liquid chromatography is D-10 auto analyser
4. ECG

B. Special Investigations-

1. Serum GGT : CARBOXY SUBSTRATE METHOD
2. Fundoscopy

STAGING OF DIABETIC RETINOPATHY[14]

NON-PROLIFERATIVE DIABETIC RETINOPATHY (NDPR)

Mild NPDR

At least one micro aneurysm.

Moderate NPDR

Hemorrhages or micro aneurysms (H/Ma), venous beading (VB), Soft exudates and intraretinal microvascular abnormalities (IRMAs) definitely present.

Severe NPDR

H/Ma in all 4 quadrants, VB in 2 or more quadrants, Intra-retinal microvascular abnormalities (IRMA) in at least 1 quadrant.

Very Severe NPDR

Any two or more of severe NPDR levels.

PROLIFERATIVE DIABETIC RETINOPATHY (PDR)

Early PDR

New vessels on the retina and definition for high-risk PDR not met.

High-Risk PDR

New vessels on the disc of 1/4 to 1/3 or more of the disc area or any new vessel and vitreous or pre-retinal or vitreous hemorrhage.

CLINICALLY SIGNIFICANT MACULAR OEDEMA (any one of the following):

- Thickening of the retina located 500 μm or less from the center of the macula.
- Hard exudates at 500 μm or less from the center of the macula with thickening of the adjacent retina.

- A zone of retinal thickening, one-disc area or larger in size, any portion of which is one-disc diameter or less from the center of the macula.

DIAGNOSIS

DR was diagnosed by using a direct ophthalmoscope.

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 $P \leq 0.05$.

RESULTS:

TABLE – 1 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 – 2 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.

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TABLE – 3 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 – 4 COMPARISON OF STUDY VARIABLES AMONG DIABETES RATINOPATHY [N=100 (CASES)]

	RATINO--PATHY	N	Mean	S.D.	Mean differences	P value
HBA1C	Absent	65	8.14	1.13	1.81	0.001 (S)
	Present	35	9.95	0.74		
SGGT	Absent	65	48.32	8.57	10.47	0.001 (S)
	Present	35	58.8	7.77		

In Case group (total=100), mean score of HBA1C, SSGT and were higher in diabetes retinopathy as compared to without diabetes retinopathy which showed statistically significant results.

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GRAPH – 1 COMPARISON OF STUDY VARIABLES AMONG DIABETES RATINOPATHY [N=100 (CASES)]

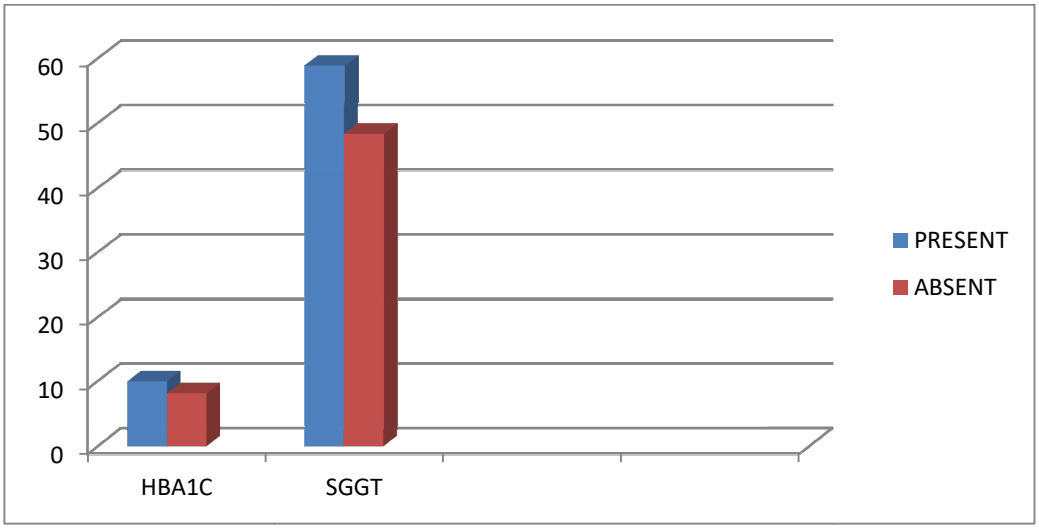

TABLE – 5 COMPARISON OF DIABETES RETINOPATHY AMONG GROUPS

			Diabetes Retinopathy		Total
			Absent	Present	
Groups	Case	N	65	35	100
		%	65.0%	35.0%	100.0%
	Control	N	98	2	100
		%	98.0%	2.0%	100.0%
Total		N	163	37	200
		%	81.50%	18.5.0%	100.0%

X^2=12.34, df=1, P value=0.001 (S)

35% of patients were found in case while only 2% of patients were found in control group. Comparison of retinopathy with groups showed statistically significant results.

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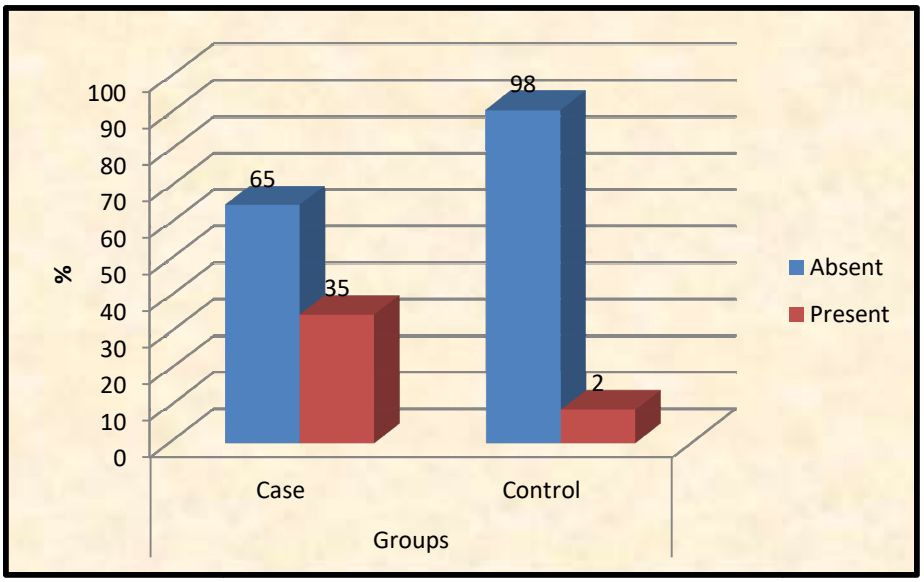
GRAPH - 2 COMPARISON OF DIABETES RETINOPATHY AMONG GROUPS



DISCUSSION:

It has been estimated that 30% of people with DM have DR worldwide[15]. A pooled analysis of 35 studies showed that the overall prevalence of DR of any severity is 34.6% and the prevalence of proliferative diabetic retinopathy (PDR) and diabetic macular edema (DME) is 6.96% and 6.81% respectively. The presence of diabetic retinopathy is directly proportional to the duration of DM.

Based on our study serum GGT levels are significantly higher in DM patients with retinopathy compared to DM patients without retinopathy. It can be useful in practice to identify DM subjects who are at risk of retinopathy. In another study conducted in Central Africa in 2010, Type 2 diabetic patients with retinopathy compared to diabetic patients without retinopathy and non-diabetic patients had significantly higher levels of GGT levels, which is in agreement with our study results[16].

It is a retinal microvasculopathy which results from prolonged hyperglycaemia. Increase in the duration of diabetes increases the prevalence of DR. It is a progressive condition with micro vascular alterations that lead to retinal ischemia, retinal permeability, retinal revascularization and macular edema[13.] After about 20 years, retinopathy develops in almost all patients with type1 and in 60% with type 2 DM.. The major risk factors for the onset and progression of DR are duration of diabetes, degree of glycaemic control, hypertension, and hyperlipidemia.

DR is asymptomatic in the initial stages. Hence, it is recommended that annual dilated fundus examination be performed in all patients with type 1 DM till they develop signs of retinopathy. But fundus examination should be performed at the time of diagnosis among patients with type 2 DM since the onset and duration of the disease is unknown. Thereafter depending on the severity of the DR, fundus examination may be done.

CONCLUSION:

The present study has shown that oxidative stress and serum GGT are some of the factors associated with diabetic micro vascular complications (Retinopathy). 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 fundoscopy should be routinely performed at regular intervals for earlier detection of diabetic micro vascular complication.

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