



Comparison of Liver Enzymes (ALT, AST & GGT) in Patients with Newly Diagnosed and Established Type-2 Diabetes Mellitus in Rural Population of Northern India

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Abstract

Background: Work on the comparison of liver enzymes between newly diagnosed type-2 diabetes mellitus (T2DM) and established T2DM can be an indicator of insulin resistance.

Objective: To compare the serum levels of alanine amino transferase (ALT), aspartate amino transferase (AST), and γ -glutamyl transferase (GGT) in patients with newly diagnosed and established T2DM in rural Jaipur (India).

Material and Methods: A cross-sectional study comprises with 240 subjects, divided into three groups of 80 each including control. (a): 80-newly diagnosed type-2 DM, (b): 80-established T2DM and (c): 80-healthy age and sex matched controls. Fully automated analyser (HUMAN) was used for biochemical analysis of FPG, ALT, AST, GGT. Chi square (χ^2) test and Z-test were used for statistical analysis. $P < 0.05$ was considered as significant.

Results: Highly significant association was found between newly diagnosed T2DM with raised ALT/ raised GGT, and no significant association was found between newly diagnosed T2DM and raised AST with compare to established T2DM.

Conclusion: Rise of ALT and GGT in newly diagnosed T2DM represents insulin resistance due to accumulation of fat in hepatocytes and indicates more oxidative stress due to lipid per-oxidation, β -oxidation. Rise in AST is nonspecific to liver involvement in T2DM and might be due to other manifestations.

Keywords: Liver enzymes ALT, AST, GGT, T2DM.

Introduction

Diabetes mellitus (DM) is a major public health problem in India and worldwide. There are two main types of DM. Type-1 DM and Type-2 DM, Where type-1 DM is caused by autoimmune destruction of insulin producing β -cells in the

pancreas result in absolute insulin deficiency and type-2 DM is characterised by raised insulin resistance, raised glucose production, abnormal fat metabolism^[1]. The prevalence of T2DM is 11% in urban and 2.4% in rural area and is on persistently increasing trend. As a result of insulin resistance

in adipose tissue, lipolysis and free fatty acid flux from adipocytes are increased, leading to increased lipid (VLDL, TG) storage in hepatocytes^[2]. This excessive lipid storage in the liver becomes toxic to hepatocytes leading to hepatocyte injury. Insulin resistance state and steatosis also causes increase in pro-inflammatory cytokines such as tumor necrosis factor (TNF,) which causes hepatocellular injury, resulting in increased leakage of liver enzyme in the blood^[3]. Mild elevation of liver enzymes are frequently found in pre diabetic and T2DM patients^[4,5] but chronic persistent and progressive rise in liver enzymes in T2DM may suggest other cause of chronic liver disease^[6].

Material and Methods

A cross-sectional study comprise with 240 subjects, divided into three groups 80 in each including control.

(a): 80-newly diagnosed T2DM,

(b): 80-established T2DM and

(c): 80-healthy age and sex matched controls.

All 240 subjects were selected for this study after filled consent form was signed by the patients, and then history was taken followed by clinical & routine examination. Diabetes could be

provisionally diagnosed with any one of the three criteria:

- 1) Fasting plasma glucose (FPG) >126mg/dl (Fasting: no caloric intake for at least 8 hours).
- 2) Random plasma glucose (RPG)>200mg/dl with classic diabetes symptoms (↑ Urination, ↑ Thirst, ↓ weight)
- 3) Post prandial plasma glucose (PPPG) after 2 hrs of meal >200mg/dl.

Estimation of glucose was carried out by spectrophotometric glucose oxidase peroxidase (GOD-POD) method (using human kit for fully auto analyser)^[7]. AST (Ref range:10-40U/L), ALT (Ref range: 8-50U/L) and GGT (Ref range: 15-75U/L) were assessed with a Trivitron Nanolab 150TM fully automated spectrophotometer using the original kits (Centronic, Gm BH, Wartenberg, Germany).Statistical analysis was carried out by using Chi-square (χ^2) test and Z-test. P value <0.05 was considered as statistically significant.

Results

Highly significant association was found between newly diagnosed and established T2DM with raised ALT/ raised GGT. No significant association was found between newly diagnosed and established T2DM with raised AST (Table-1).

Table-1: Comparison of liver enzymes (ALT, AST and GGT) in newly diagnosed and established T2DM patients.

Test Group	Liver Enzymes		Test		Control		Total		χ^2	P-value	Significance
			N	%	N	%	N	%			
New Dig. T-2DM	S. ALT N=80	↑	18	22.5	05	06.25	023	14.37	8.5814	0.003396	Highly Significant
		Normal	62	72.5	75	93.75	137	85.63			
	S.AST N=80	↑	10	12.5	04	05	14	08.75	2.818	0.093212	No Significant
		Normal	70	87.5	76	95	146	91.25			
	S.GGT N=80	↑	25	31.25	03	03.75	028	17.5	20.9524	0.00005	Highly Significant
		Normal	55	68.75	77	96.25	132	82.5			
Esta. T-2DM	S. ALT N=80	↑	13	16.25	05	06.25	018	11.25	4.0063	0.045332	Highly Significant
		Normal	67	83.75	75	93.75	142	88.75			
	S.AST N=80	↑	07	08.75	04	05	011	13.75	0.8786	0.34859	No Significant
		Normal	73	91.25	76	95	149	86.25			
	S.GGT N=80	↑	20	25	03	03.75	023	14.38	14.6747	0.000128	Highly Significant
		Normal	60	75	77	96.25	137	85.62			

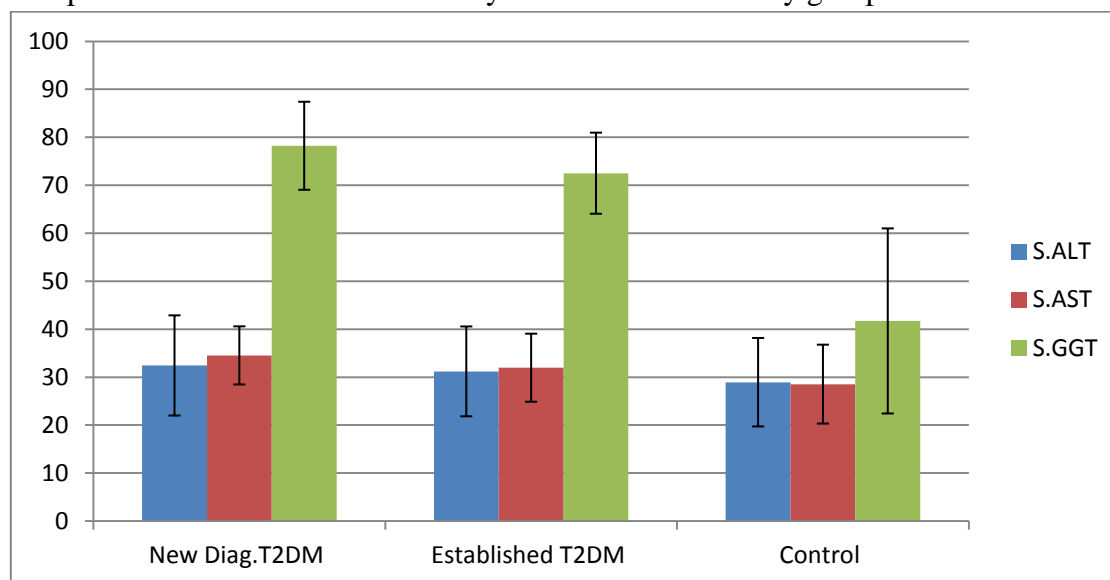
Highly significant difference was found between the mean of serum ALT and GGT levels in newly diagnosed and established T2DM (P<0.05). There

is no significance difference was found between the mean of serum AST in newly diagnosed and established T2DM (P>0.05) (Tabl-2, Graph-1).

Table-2: Mean \pm SD of Serum ALT, AST, GGT in newly diagnosed T2DM, Established T2DM and Control group

Liver Enzymes	New Diag.T2DM		Established T2DM		Control		Z-test	Sig.
	Mean	SD	Mean	SD	Mean	SD		
S.ALT	32.43	10.44	31.193	9.367	28.94	9.22	2.456	HS
S.AST	34.52	6.06	31.96	7.09	28.54	8.22	0.794	NS
S.GGT	78.22	9.176	72.5	8.45	41.71	19.29	4.106	HS

HS-highly significant, NS-no significant

Graph-1: Comparison of mean \pm SD of liver enzymes in all T2DM study groups

Discussion

ALT: In the present study, 22.5% patients of newly diagnosed T2DM were found raised serum ALT. It compared with established T2DM and controls, 16.25% patients and 6.25% subjects were found raised ALT respectably. The present study showed consistent result with a study done by Shreyas et al. they concluded, a well-defined population of newly diagnosed T2DM with high incidence of abnormal serum ALT levels which was associated with features of the metabolic syndrome but not glycemic control^[8]. Sattar et al. found ALT as continuous variable which was associated with new onset type-2 diabetes. Mean \pm SD of ALT was 20.9 \pm 7.6U/L thus elevated ALT levels predict incident diabetes^[9]. The present study showed consistent results with this study.

AST: In the present study, 12.5% patients of newly diagnosed T2DM were found raised serum AST levels. It compared with established T2DM and controls, 8.75% patients 5% subjects were

found raised serum AST respectably. The AST level was not significantly associated with type 2 DM both newly diagnosed and established. Our study is in accordance with a study done by Ahn et al. they suggested that the serum ALT concentrations were independently associated with type 2 diabetes established cases in both sexes. It also showed that there was no linear relationship between AST and type 2 diabetes^[10].

GGT: In the present study, 31.25% subjects of newly diagnosed T2DM were found raised serum GGT levels. It compared with established T2DM and controls 25% patients and 3.75% subjects were found raised serum GGT respectably. Our study also showed consistent result with a study done by Sabanayagam et al. they showed that higher serum GGT levels were positively associated with type-2 diabetes mellitus, independent of alcohol consumption, body mass index, hypertension and other confounders^[11].

Conclusion

The present study concluded that elevated serum ALT and GGT is less than two times the upper limit of normal in T2DM as compared to controls. Serum levels of ALT and GGT were found to be marginally raised in newly diagnosed as compared to established T2DM. It represents insulin resistance due to accumulation of fat in hepatocytes which is known to be directly toxic to hepatocytes. Raised ALT and GGT in newly diagnosed as compared to established T2DM indicates more oxidative stress due to lipid peroxidation, β -oxidation and accumulation of inflammatory mediators in view of initial stage of developing insulin resistance. Rise in AST is concluded to be nonspecific to liver involvement in T2DM and might be due to other manifestations.

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