A Comparative Study of Alanine Aminotransferase & Alkaline Phosphatase in Type-2 DiabeticPatients and Non-Diabetics

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Abstracts: Background: The aim of this study was to find out the liver function test abnormalities in a group of diabetic type-2 patients in Jamnagar, Gujarat and to determine the factors associated with these biochemical changes. **Method:** In this cross sectional study conducted at the diabetic clinic in GGH General Hospital, Jamnagar between May 2012 and April 2013, a total of 100 patients were included. Parameters like serum alanine aminotransferase (ALT), alkaline phosphatase (ALP) used. **Result:** Raised ALT was noted in 30 % of diabetes type -2 patients while in control group 6% had elevated value. Elevations in serum alkaline phosphatase (ALP) were found in 38 %. Mean value of ALT & ALP had no correlation with gender of the diabetes patients. **In conclusion**, abnormal liver function results are more common among diabetes patients. Elevated ALT and ALP are the markers for associated non alcoholic fatty liver disease in diabetes patients. [Gohel V NJIRM 2014; 5(5):52-56]

Key Words: DM (Diabetes Mellitus), ALT (Alanine aminotransferase), ALP (alkaline phosphatase)

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Introduction: Diabetes mellitus is one of the major non-communicable diseases and the prevalence is rising globally. Type 2 diabetes is the most common form, accounting for 90% of all cases[1]. The total number of diabetes is projected to increase from 171 million in 2000 to 366 million in 2030. Diabetes is more prevalent in men than women [2].

There exists an association between diabetes and liver injury. Liver plays a major role in the regulation of carbohydrate homeostasis. Hepatocellular glycogen accumulation leads to hepatomegaly and liver enzyme abnormalities in poorly controlled diabetes patients. In hyperglycemic states, there will be intracellular glycogen accumulation in the hepatocytes due to increased glycogen synthesis, causing typical biochemical findings of mild to moderately elevated aminotransferases, normal liver synthetic function, with or without mild elevations of alkaline phosphatase. All these biochemical disturbances and hepatomegaly are found to be reversible with good glycemic control [3].

Secondly, liver can be affected by steatosis or accumulation of fat, a condition known as non-alcoholic fatty liver disease (NAFLD). It is a well-recognized complication of diabetes with frequency of 40–70%[4]. The steatosis is either microvesicular or macrovesicular and is found to progress to fibrosis and cirrhosis. The most common clinical finding is hepatomegaly, with normal or only mildly elevated transaminases and normal bilirubin these changes are not reversible with sustained glucose control [4]

Non-alcoholic fatty liver disease (NAFLD) is the main cause of chronic liver disease associated with diabetes and obesity. Without treatment, compensated steatosis in NAFLD will eventually lead to decompensated steatosis with necroinflammation and fibrosis, i.e stage of non-alcoholic steatohepatitis (NASH). NASH is a leading cause of end-stage liver disease and also a contributor of cardiovascular disease in type 2 diabetes mellitus [5].

Definitive diagnosis of NASH requires liver biopsy. Lifestyle modification is the gold standard in the management of NASH. Serum amino transferases such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) indicate the concentration of hepatic intracellular enzymes that have leaked into the circulation. These are the markers for hepatocellular injury and are used as primary screening of NASH [6]. Chronic mild elevations of ALT and AST are seen in type 2 diabetes patients.

Material and Methods: This study was a hospital based cross sectional descriptive study conducted

at the diabetic clinic of G.G.H. Hospital, Jamnagar between May 2011 and May 2013. Subjects were recruited according to simple random sampling method meeting the selection criteria.

Inclusion Criteria: The patients with confirmed diabetes mellitus or newly diagnosed diabetes mellitus by WHO criteria (1999), fasting plasma venous glucose of 126 mg/dl or random or two hour post prandial plasma venous glucose of 200 mg/dl.

Exclusion Criteria: The diabetic patients with history of alcohol intake, hepatotoxic drugs like amiodarone, antituberculous drugs, history of liver diseases or clinical evidence of acute hepatitis, those who were found to have evidence of hepatitis B and C virus infection (HBsAg positive and HCV antibody positive) were excluded from this study. Not willing to participate in study. Having liver and/or biliary diseases. Pregnant females for exclusion of gestational diabetes.

Subjects were explained the purpose and protocol of the study. After informed consent, blood sample were collected to measure following liver function parameters: RBS (Random blood sugar), Serum ALT (alanine aminotransferase),Serum ALP (Serum Alkaline phosphatase)

Statistics: Mean & SD were calculated. Unpaired student's 't' test was applied to test difference between means. Pearson Correlation co-efficient (r) was calculated to test correlation between parameters. Statistical significance was accepted at P value of <0.05.

Investigations were done using following Method: Random blood sugar (RBS) was estimated by Glucose Oxidase-Peroxidase (GOD-POD) method (enzymatic colorimetric test). Serum ALT was estimated by IFCC method without pyridoxal phosphate & kinetic UV method. Serum ALP was estimated by enzymatic diethanolamine buffer Kinetic method

Result: Study includes 100 diabetic subjects and 100 age and sex matched controls.

Table 1:General Characteristics of Study Groups.

	Diabetics (N=100)	**Control (N=100)**
Age(Years)	47 ± 11.11	47.01±12.65
Sex ratio (Male/Female)	68/32	68/32
Duration of DM (years)	**9.99 ±4.61**	--------

As shown in Table – 1, out of 100 patients 68 (68%) were males and 32(32%) were females & out of 100 control, 68 (68%) were males and 32 (32%) were females & average of age in both the groups is similar. Average duration of diabetes in patients is about 10 years.

Table 2: Comparison Of Liver Function Tests in Diabetics and Controls (Values Are Mean ±SD)

	Diabetics (N=100)		Control (N=100)	
	Mean	±SD	Mean	±SD
RBS (mg/dl)	174.24	31.2	97.02	15.2***
Serum ALT (U/L)	35.25	8.59	21.89	7.73***
Alkaline phosphatase (U/L)	140.26	61.36	135.26	47.77

***P<0.001

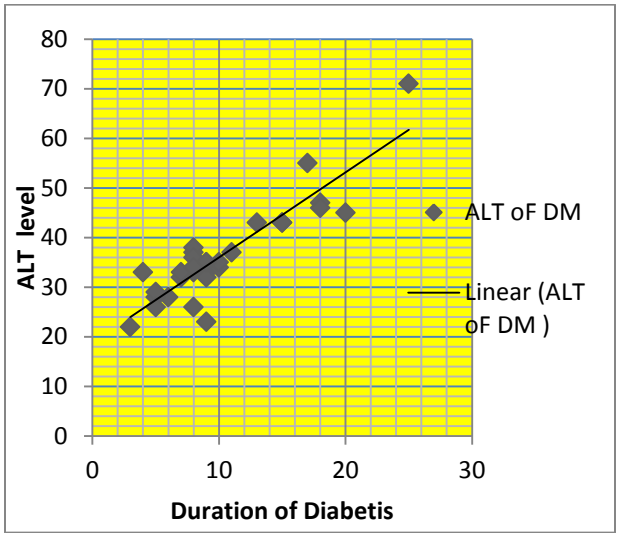
Table 2 shows, there is significant raised in level of RBS & serum ALT levels in diabetic patients as compare to control group. While there is not significant changes in alkaline phosphatase level in both study groups.

Table3: Comparison of liver function tests in male and female diabetics (values are mean ±SD)

	Male (N=68)		Female (N=32)	
	Mean	±SD	Mean	±SD
Age(years)	54.6	14.3	53.7	15.83
RBS (mg/dl)	154.33	28.49	178.5	23.50
Serum ALT (U/L)	36	10.38	33.9	11.98
ALP (U/L)	187.33	95.98	167.1	29.86

Table – 3shows, there is not significant changes in level of RBS, serum ALT & ALP levels in diabetic male & female patients.

Graph1: Correlation of Duration of DM WithSerum ALT Level



(r=0.58) (P<0.01)

Pearson Correlation co-efficient (r) was calculated to test correlation between duration of DM & serum ALT level.

It shows positive correlation between them. So, as the duration of diabetes increases serum ALT level is also increase.

Table:-3Alanine Aminotransferare

ALT	**Diabetics** (N=100)	**Control** (N=100)
<40 U/L (Normal)	70	94
>40 U/L (Elevated)	30	6

The chi squre value is 19.512 at degree of freedom 1 the p value is 0.00011, so the test result is highly significant, it proves that in diabetic patients has elevated serum ALT level in comparison with control group.

Table:-4 Alkaline Phosphatase

Alkaline Phosphatase	Diabetics (N=100)	Control (N=100)
<125 U/L (Normal)	62	88
>125 U/L (Elevated)	38	12

This study shows that elevations in serum alkaline phosphatase were found in 38 % (n = 50), p value of this study is 0.002 so it is highly significance that patient with type-2 diabetes has higher level of serum alkaline phosphatase level in comparison with non diabetics.

Discussion: Type 2 diabetes patients have been reported to be associated with higher incidence of abnormal liver function tests (LFT) compared to the individuals without diabetes, elevated ALT being the most common abnormality.

In our study population patients with elevated levels of serum ALT were significantly higher compared to controls. it proves that in diabetic patients has elevated serum ALT level in comparison with control group.

However study by J.WEST conducted in Queen's Medical Centre University Hospital, Nottingham NG7 2UH, UK also show significantly higher serum ALT in patients as compare to controls. In J.WEST's study 12.1 % of patient has elevated Serum ALT level. And p value of the J.WEST's test is < 0.001 so it is highly significant that patient with type-2 diabetes has higher level of serum ALT level in comparison with non-diabetics.

Similar study conducted in South African black & Indian adult patients with type -2 diabetes mellitus by Paruk IM[11] shows elevated serum ALT and Study conducted by han Ni[12] in Singapore General Hospital, Singapore &Ayman S. Idris[8] in International University of Africa, Sudan showed significantly higher serum ALT levels in patients compared to controls.

Study	Percentage of elevated ALT level
My study	30%
J.WEST	15.5%
Parak IM	15.3%
AymanS.Idris	12%
Han Ni	18.5%

In comparison with other studies my study shows higher percentage of elevated serum ALT level, possible reason is that in my study patients does not control their blood glucose level properly so there are more chance of high glucose level. High glucose level for prolong period is more prone to

liver toxicity and liver injury leads to release of ALT and other enzymes in the circulation so level of liver enzymes are increased.

Cut of value	Sensitivity	Specificity	Accuracy (reliability)
25	76.27	87.80	81
27	81.90	85.26	83.5
28.66	84.21	80.95	82.5
30	88.75	75.82	81
32	87.23	61	67.50
35	87.32	61	67.50

The above table shows the different cut-off value of the serum ALT considering the above range represents the diabetic and below value suggests the non-diabetic.

If we set the cut off value at 28.66 than that sensitivity and specificity of the test is good along with good accuracy. But if we set cut off value at 27 than sensitivity of the test decreased associated with increasing the accuracy or reliability of the test.

If we set cut of value at 25 there is very much less sensitivity but good specificity

If we set cut off value at higher level than sensitivity of the test is increased while specificity of the test is compromised associated with Accuracy. So table indicate that if we set cut off value at higher level ability of the test to detect true positive is increased while if we set cut off value at lower level than the ability of the test to detect true negative as negative is increased

In our study population patients with elevated levels of serum alkaline phosphatase were significantly higher compared to controls. it proves that in diabetic patients has elevated serum alkaline phosphatase level in comparison with control group.

However similar study was conducted by Paruk IM s[11] in ObafemiAwolowo University, Ile-Ife, Nigeria & by ShobhaLuxmi[7] in the medical outpatient department of Jinnah postgraduate medical centre, Karachi from September 2006 to March 2007 show significantly higher serum alkaline phosphatase in patients as compare to controls So my study is completely tune with by ShobhaLuxmi[7] &Paruk IM[11]

Conclusion: Type-2 Diabetes mellitus is a syndrome of impaired carbohydrate, fat, and protein metabolism caused by decreased sensitivity of the tissues to insulin.

The liver plays a major role in the regulation of carbohydrate metabolism, it has the capability to store glucose as glycogen and also synthesize glucose from non-carbohydrate sources.

This function of liver makes it vulnerable to diseases in subjects with metabolic disorders particularly Diabetes mellitus.

So, Individuals with type 2 diabetes have a higher incidence of LFT impairment than individuals who do not have diabetes. The most common alteration is elevated ALT. The duration of DM significantly correlates with ALT levels. Insulin resistance in DM type-2 affecting liver metabolism is probably altering liver function tests

Limitation of This Study And Future Research: Larger Sample size would be more conclusive. Study of other confounding factors like effect of anti-diabetics and lipid modifying drugs may be helpful. Study involving follow up of high risk subjects over long duration would be more useful in identifying the causative role of diabetes in liver function impairment.

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