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Research Article

SERUM ALANINE AMINOTRANSFERASE (ALT) ACTIVITY AMONG DIABETIC PATIENTS

Anshu Upadhayay*

Nepal Institute of Health Sciences, Gokarneshwor , Kathmandu, Nepal

*Email: upadhayayanshu@gmail.com

Abstract

Serum Alanine aminotransferase (ALT) activity is the most common screening test as a part of routine assessment of liver damage. Due to its low activity in extra hepatic tissues an increase in serum ALT is more specific for liver disease. The liver pathology among diabetics is similar to that of alcoholic liver disease, including fatty liver, steatohepatitis, fibrosis, and cirrhosis. Thus, elevated serum ALT activity which is a common sign of liver disease is also observed more frequently in diabetics. This study has been designed with the aim to determine the association of serum ALT activity with diabetes mellitus. The study included 208 subjects attending Nepal police hospital during the time frame 6th October 2009 to 4th January 2010.The ALT activity in serum was determined by kit method, fasting and post prandial sugar was tested by GOD-POD method.

Among the total diabetic subjects 43.26% were found to have elevated serum ALT activity (>40IU/L). Diabetic status was found to be significantly associated with ALT activity (p=0.04). In addition to diabetic status body mass index (BMI) was also significantly associated with ALT activity (p=0.02) and higher BMI increases the likelihood of elevated ALT. The association of ALT activity was found to be inverse and significant with age of the patient(r=-0.217, p=0.005). Physical activity was also found to be inversely associated with ALT activity(r=-0.149, p=0.03).

Keywords: Alanine aminotransferase; Diabetes; serum glutamate pyruvate transferase; ALT

Introduction

Alanine aminotransferase (ALT) is a cytoplasmic enzyme; it has an important role in gluconeogenesis and amino acid metabolism. ALT catalyses the transamination reaction of alpha ketoglutarate and L-alanine forming glutamate and pyruvate. The highest ALT activity is found in hepatocytes for this reason it is the most specific marker of liver disease in clinical practice(Stone and Van Thiel, 1985). Increased serum ALT activity can suggest hepatocellular injury or necrosis of striated muscle. In liver disease associated with hepatic necrosis such as viral hepatitis, serum ALT activity is elevated before the clinical signs and symptoms of disease such as jaundice appears.

The liver pathology among diabetics is similar to that of alcoholic liver disease, including fatty liver, steatohepatitis, fibrosis, and cirrhosis (Schindhelm *et al.*, 2006). Thus, elevated serum ALT activity which is a common sign of liver disease is also observed more frequently in diabetics. The relationship between elevated ALT level and Diabetes has been linked with Non-alcoholic fatty liver disease and Insulin resistance (Banerji *et al.*, 1995). Serum ALT activity which reflect liver fat content, have shown to be associated with diabetes risk, independently of alcohol consumption and other possible factors like high BMI, smoking habit(Sattar *et al.*, 2004). Raised ALT which reflects fatty change in the liver in turn reflects pathophysiological changes predating the development of diabetes. The study has been designed with aim to determine the association of ALT activity with diabetic status and to clarify the factors contributing to ALT elevation. The association may help in management of diabetes and prevent the complication.

Material and Methods

In this study 208 Patients attending Nepal Police Hospital during the time frame 6th October 2009 to 4th January 2010 were categorized as Diabetic and Non diabetic based on medical records. The information on Tea/coffee consumption, Alcohol intake, smoking status, physical activity and history of Gall stone either present, absent or operated was collected from self-structured questionnaire

survey. Patients with suspected jaundice were excluded from the study.

The BMI was calculated by measuring the height and weight of each participant and was expressed as kg/m^2. After overnight fasting of 12 hours, 5ml of blood was collected from each patient by vein-puncture. The separated serum was used for the analysis of Serum Alanine aminotransferase activity, Fasting sugar and post prandial sugar by kit method. Serum ALT activity >40IU/L was considered abnormal. All statistical analysis was performed using SPSS 11 Software. P value <0.05 was considered statistically significant.

Results and Discussion

The study comprises 208 subjects visiting Nepal police hospital during the time frame 6th October 2009 to 4th January 2010. Based on the diabetic status subjects were classified as Diabetic and Non -Diabetic. Among the total subjects studied 68% were diabetic and 32% were Non-Diabetic (Table 1**)**. An elevated ALT is considered a consequence of hepatocyte damage, and is observed more frequently among diabetics (Ruhl *et al.*, 2003;Clark *et al.*, 2003). In the present study among total diabetic subjects 43.26% were found to have elevated ALT activity (Table 2). Likewise in the study by Arthur and colleagues (Meltzer *et al.*, 1986) ALT activity at least twice the upper limit of normal of 43IU/L was found to be more common among diabetics. Increased gluconeogenesis, owing to increased conversion of alanine to glucose, is suggested as important mechanism for the up regulation of ALT enzyme activity in diabetic subjects (Consoli *et al.*, 1990).

Table 1: Characteristics of study population

Characteristics	**Diabetic Mean ±S.D**	**Non Diabetic Mean± S.D**
Age (years)	53.771±1.98	38.25± 12.70
BMI(kg/m2)	24.61± 3.71	24.25 ±3.81
Fasting sugar(mg/dl)	133.0± 50.1	84.29± 9.58
Post prandial sugar(mg/dl)	203.2± 81.34	102.0± 2.82
Serum ALT activity(IU/L)	42.95 ±26.73	35.88 ±16.87

The mean value of Age, BMI, Fasting sugar, Post prandial sugar and Serum ALT activity in Diabetic and Non diabetic subjects (n=208).

The present finding in accordance with other studies (Vozarova *et al.*, 2002; Hanley *et al.*, 2004; Sattar *et al.*, 2004; Wannamethee *et al.*, 2005) showed a significant association of ALT activity with diabetic status (p=0.04). The putative role of the liver in the pathogenesis of diabetic mellitus, and impaired hepatic insulin signaling as a consequence of fatty infiltration in the insulin resistant state is posed as an important pathophysiological mechanism for associating ALT activity with diabetes mellitus(Schindhelm *et al.*, 2006).

Table 2: Frequency of elevated ALT in diabetic and Non-Diabetic

Diabetic status	**No. of subjects(n)**	**Elevated ALT activity n (%)**
Diabetic	141	61(43.26%)
Non – Diabetic	67	23(34.3%)

Among total diabetic subjects (n= 141) 43.26% had elevated ALT activity.

The study also found a significant inverse co-relation between age and ALT activity (r=-0.217,p=0.005*),the mean ALT activity was found to be decreased with increasing age group with peak at 40-59 years of age group in Diabetics (Table 3). Similar co relation between age and ALT activity was reported by previous report, where an inverted U like relation of ALT and age was revealed (Elinav *et al.*, 2005). Some studies have reported significant association of ALT activity with gender, in the current study a significant difference in ALT activity with gender was found only among Non-Diabetics at p=0.005. The mean ALT activity was higher in men than in women among Non-diabetics similar to the study by Leclercq *et al*. (1999) where the mean ALT activity was higher in men than in women.

Table 3: Co -relation of ALT activity with different parameters

Parameters	**Pearson co-relation coefficient (r)**	**P value**
Age	-0.217**	0.005
BMI (kg/m2)	0.164*	0.02
Alcohol consumption	0.007	0.19
Smoking status	-0.006	0.392
Tea / coffee consumption	-0.002	0.234
Physical activity	-0.149*	0.039
Gall stone	0.061	0.237
Fasting glucose level	0.007	0.467
Post prandial glucose level	0.009	0.456

**co relation is significant at 0.01 level (1 tailed)
*Co relation is significant at 0.05 level (1 tailed)

In accordance with previous studies, the present study found factors in addition to diabetes associated with ALT activity (Table 4).

The majority of previous studies (Sakugawa *et al.*, 2004; Nanji *et al.*, 1986) have shown significant positive association of BMI with ALT. The present result is also in consonance with these studies and a significant positive co relation of ALT activity with BMI was found (r=0.164*,p=0.02). The mean ALT activity was found to be

increased with degree of obesity. In the analysis of National health and Nutrition examination survey (NHANES) elevated ALT was significantly associated with higher BMI.

Table 4: Association of ALT activity with Diabetic status

Diabetic status	Mean ± S.D	P value
Diabetic	42.95±26.73	0.04
Non – Diabetic	35.88±16.87	

ALT activity was significantly associated with Diabetic status at p=0.04.

Likewise in study by sakaguwa et al(Sakaguwa *et al.*, 2004) the mean ALT activity was found to be increased with degree of obesity. ALT was more clearly related to BMI in the study by Wejstal *et al.* (1988). Insulin resistance, increased pro-inflammatory cytokine production, Non-alcoholic fatty liver disease, oxidative stress and mitochondrial dysfunction leading to hepatocyte damage/destruction, have all been posed as important pathophysiological mechanism (Schindhelm *et al.*, 2006) causing elevated ALT in obese subjects.

Age and physical activity was negatively co related with ALT at 1% and 5% level of significance respectively. BMI was positively co related with ALT at 5% level of significance. Alcohol consumption, Fasting glucose level, post prandial glucose level, Gall stone showed no significant association with ALT.

The ALT activity was significantly different between the age groups 40-49, 50-59, 60-69 and >70 in diabetic and Non diabetic subjects. However, the ALT activity was not significantly different within the age groups (p=0.172&0.05) respectively in diabetic and Non diabetic subjects (Table 5).

Table 5: Age wise comparison of ALT activity

Age group (years)	**Diabetic**	**Non - Diabetic**	**P value (t-test)**
	Mean± S.D	Mean± S.D	
20-29	41.5 ±9.1	29.4 ±14.23	0.32
30-39	48.0 ±24.3	37.3 ±17.26	0.05
40-49	50.7± 31.5	41.3 ±18.09	0.005
50-59	42.5± 28.2	25.33± 8.47	0.003
60-69	36.4± 21.9	28.66± 10.4	0.006
>70	33.5 ±17.6	55.5± 4.94	0.009

The ALT activity was significantly different in Female diabetic and Non diabetic subjects at p= 0.005. A significant difference in ALT activity was observed between Male and Female in Non-diabetics (p=0.005), but not among Diabetics (p=0.839) (Table 6).

Table 6: Gender wise comparison of ALT activity

Gender	**Diabetic**	**Non-Diabetic**	**P value (t- test)**
	Mean± S.D	Mean± S.D	
Male	42.6±25.5	38.7±16.5	0.24
Female	43.8±30.3	25.1±14.08	0.005
	P = 0.839	P=0.005	

The ALT activity was significantly different in Diabetic and Non diabetic with BMI between 25-30 kg/m^2 at p=0.02.The ALT activity was not significantly different among the age groups (p=0.175 & 0.25) respectively in diabetic and Non diabetic subjects (Table 7).

Table 7: ALT activity according to BMI grading

BMI grading (kg/m^2)	**Diabetic**	**Non - Diabetic**	**P value (t- test)**
	Mean± S.D	Mean± S.D	
<25	39.78±28.57	33.22±15.92	0.06
25-30	48.34±23.24	39.65±17.99	0.02
>30	49.7±16.63	43.33±19.30	0.64

ALT activity was significantly different in Non-alcoholic, Non-smoker and Tea and coffee consumer Diabetic and Non diabetic subjects with p value 0.01, 0.005 and 0.03 respectively. ALT activity was significantly different in Non-diabetic Alcoholic and Non Alcoholic subjects (Table 8).

A significant inverse co relation of ALT activity with physical exercise (r=-0.149*, p=0.039) was found in the present study. Frequency of physical activity was found to be inversely associated with ALT in the study by Debbie et al (Debbie *et al.*, 2005). Few other studies (Suzuki *et al.*, 2005; Hickman *et al.*, 2004) have also postulated an inverse association of ALT with physical activity where the association of ALT with physical activity were based on amount of weight loss and in these studies ALT remained significantly lower in those patients who maintained their reduced weight. Physical activity improves insulin sensitivity and reduces oxidative stress leading to decreased ALT activity.

A non-significant inverse relation between Tea/coffee consumption and ALT activity was found (r=-0.002,p=0.234) which resembles the finding by Meltzer et al(Meltzer *et al.*, 1986) where the risk of elevated ALT activity declined with increasing intake of coffee leading to speculation regarding the possible beneficial effects of Tea/coffee on the liver. Coffee consumption was inversely related with serum level of liver enzymes in the study including Japanese men and women (Ikeda *et al.*, 2010).

Table 8: ALT activity according to Tea Coffee consumption, Smoking status, drinking habit

	Diabetic Mean± S.D	**Non - Diabetic Mean± S.D**	**P value (t- test)**
Alcoholic	44.5±27.4	39.4±17.2	0.205
Non- Alcoholic	40.62±25.7	29.4±14.3	0.01
	p=0.38	p=0.01	
Smoker	41.25±26.07	40.6±18.1	0.906
Non- Smoker	44.5±27.4	33.0±15.6	0.005
	p=0.46	P=0.08	
Tea/ Coffee consumer	42.7±27.2	45.3±18.3	0.03
Tea / Coffee non consumer	33.0±15.6	24.0±0.00	-
	p=0.70	-	

In the current study, alcohol consumption showed a non-significant association with ALT similar to the study performed in Japan (Nakamura *et al.*, 1998; Nakamura *et al.*, 1980). A 4 year follow up study in Korea also demonstrated that the risk for elevated ALT values over the four years increased with the BMI changes (Duk-Hee *et al.*, 2001), but not with alcohol consumption.

In a study by Meltzer (Meltzer *et al.*, 1986) increased alcohol consumption showed positive but not statistically significant association with ALT.

However, in the study on Danish Population as well as a study based on male in London reported the raised level serum liver enzymes with self-reported alcohol consumption(Steffensen *et al.*, 1997; Whitehead *et al.*, 1996). This could be because the total alcohol consumption in our subjects might have been lower than in other studies.

Similarly, presence of Gall stone also showed a non-significant association with ALT similar to the study by Arthur et al(Meltzer *et al.*, 1986).

Cigarette smoking may play a role in liver function abnormality and/or specific liver disease. In a on healthy male workers(Chan-Yeung *et al.*, 1981). However, in the current study and similar to another report this correlation was not significant (Jang *et al.*, 2012; Meltzer *et al.*, 1986; Whitehead *et al.*, 1996).

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