A QUEST FOR NORMAL VALUES OF SERUM AMINOTRANSFERASE AND ITS ASSOCIATION WITH AGE AND BODY MASS INDEX

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ABSTRACT

Objective: To determine the reference range for serum alanine aminotransferase (ALT) levels for young healthy individuals in our population and to find out effects of age and body mass index on alanine aminotransferase.

Study Design: Descriptive cross sectional study.

Place and Duration of Study: Military Hospital Rawalpindi; from Dec 2009 to April 2010.

Material and Methods: Five hundred and fifty three young healthy adults were included in the study. Detailed history was taken. Parameters like Age, height and weight were measured. Relevant investigations were carried out for each subject which included blood complete picture, Chest X-Ray, ECG, Urine routine examination, liver function tests, serum urea, serum creatinine, serum uric acid, plasma glucose (F), Anti HCV antibodies, HBsAg, HIV antibodies and VDRL. Data was analyzed using SPSS version 22.

Results: Age of subjects ranged from 19 to 50 years (29 ± 6) years, BMI 15.59 to 29.8, (21.58 ± 2). Serum alanine aminotransferase ranged from 17 to 81 IU/l, (29.9 ± 8) IU/l. Serum alanine aminotransferase for subjects with body mass index more than 25 Kg/m2 was 29.6 ± 7 IU/L. There is no significant difference in value of mean ALT overall and in those with BMI of more than 25 (p=0.149)

Conclusion: Mean serum alanine aminotransferase value in young healthy adults included in this study was 29.9 ± 8 IU/L which is lower than normal reference provided at present which is 40 IU/l. Statistical analysis revelaed that serum ALT is not significantly influenced by age and BMI.

Keywords: Serum alanine transaminase (ALT), Body mass index (BMI).

INTRODUCTION

Chronic liver disease (CLD), if not detected and managed at an early stage can progress to cirrhosis. Serum ALT and aspartate aminotransferase (AST) are measured during routine examinations to detect CLD. Medical practincinors use the laboratory reported ALT upper reference limit (upper limit of normal [ULN]) or its multiple (eg, 1.5_ULN) to proceed for the further evaluation which can be expensive and invasive, however ignoring aminotransferase elevations can allow liver disease to progress if not recognized and managed at an early stage. Therefore, ALT ULN is very important in determining the risk-benefit ratio of further evaluation which is expensive but essentially required in such cases[1].

ALT level is used as a marker of liver diseases and is important in deciding which patients require therapy in diseases like chronic hepatitis due to Hepatitis B infection. Raised ALT levels do not always correlate well with Liver cell necrosis. Many patients are not identified by ALT levels despite having necro-inflammatory activity and fibrosis, as seen in Hepatitis C[2,3]. Moreover, ALT levels can vary with BMI, gender, deranged lipid and carbohydrate metabolism and the circadian variations[4,5]. ALT can be within the normal limits in patients with CLD[6,7]. Presently a debate is going on whether to lower the normal range of aminotransferases to accommodate the changing lifestyle factors that affect aminotransferase concentrations, especially obesity, which would increase the detection of Hepatitis C and fatty liver disease[2,8].

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Because of sample stability issues, validated standards are not used to establish a ULN for aminotransferases[9]. Mostly laboratories establish their own reference ranges from local/defined populations[10].

In a study conducted in America, to establish the variability in the upper limit of normal (ULN) for alanine aminotransferase (ALT) across different laboratories, it was found that there is wide variability in ALT ULN across different laboratories[11]. Present study was designed and conducted to find out the reference range for ALT for young healthy individuals of our population and to its relation with BMI and age.

Table-1: Statistical parameters of age, alanine aminotransferase and body mass index on. (n=547).

Variable	Mean±SD	Standard error	Median	Mode	Minimum	Maximum	Range
Age	29.69 ± 6.34	0.27	28	25	19	50	31
ALT	29.98 ± 8.02	0.34	28	27	17	81	50
BMI	21.56 ± 2.10	0.09	21.56	21	15.59	29.80	14.21

Table-2: Regression coefficients along with significance (n=547).

Variable	Unstandardized coefficients		Standardized coefficients	t	*p*-value
	B	Standard error	Beta		
Age	-.039	.055	-.031	-.713	.476
BMI	.240	.166	.063	1.446	.149

MATERIAL AND METHODS

This descriptive cross sectional study was carried out in Gastroenterology Department of Military Hospital Rawalpindi from December 2009 to April 2010. During the study period a total of 553 subjects were recruited through convenience non probability sampling technique. Young healthy adults reporting for medical examination either before joining service or going abroad were included in the study group. Those already diagnosed or found to be suffering from viral hepatitis, nonalcoholic fatty liver disease or systemic diseases like diabetes mellitus or ischemic heart disease were excluded from the study. Detailed history was taken and findings on investigation were documented, including age, height and weight. Investigations carried out in each case included blood complete picture, Chest X-Rays, ECG, Urine Routine Examination, serum liver function test, urea, creatinine, uric acid, plasma glucose, serology for Anti HCV antibodies, HBsAg, HIV and VDRL. Data was analyzed using SPSS version 22. Mean and standard deviation of age, BMI and ALT were calculated. Effects of age and BMI on serum ALT was calculated using multiple linear regression. A *p*-value of < 0.05 at confidence level of 95% was identified as significant.

RESULTS

During the study period a total of 553 persons were enrolled. The age ranged 19 to 50 years (29 ± 6) years (table-1). ALT ranged from 17 to 81 IU/l, with a mean 29.9 ± 8 IU/l. BMI was between 15.59 and 29.8, with mean 21.58 ± 2, (table-1). ALT for subjects with BMI of more than 25 Kg/m2 was 29.6 ± 7 IU/L. There was no significant difference between mean ALT values of subjects with BMI more than 25 Kg/m2 and mean ALT values of other subjects (*p* value *p*=0.149). However, subjects with BMI more than 25 were very small fraction of whole study subjects, just 5.2%.

Descriptive statistics for age, ALT and BMI are shown in table 1. Adjusted R square was 0.001 and the ANOVA statistics were, F=1.14 and *p*-value = 3.1. Output of multiple linear regression showed that the model was not significant. Detailed regression statistics along with regression coefficients are shown in table-2. The p-values of age (*p*=0.476) and BMI (*p*=0.149)

show that these two variables have no predictive effect on ALT.

DISCUSSION

Since ALT levels have been used as a marker to detect unsuspected liver disease and for treatment decisions in many chronic liver diseases like chronic Hepatitis B, there have been healthy debate on ALT level in healthy persons/blood donors. One of the earliest study was carried out by Leclercq in 1999 to find out the influence of body mass index and sex on serum ALT levels in healthy blood donors. They found out that the mean serum ALT for men were 26.8 IU and the mean BMI for males was 24.4Kg/m2.They concluded that there was a positive correlation between ALT levels and BMI irrespective of sex of the blood donors[12]. In our study mean value for ALT for young adults was 29.9 ± 8 IU/L, which like above referred study is lower than normal reference provided by laboratory.

Another land mark study was published by Prati et.al. in 2002,[2] to acess the reference range for serum ALT in healthy Italian subjects. Study included 6000 subjects who were healthy blood donors. Their updated upper limit of serum ALT for men was 30 U/L,much lower than 40 U/L,considered normal at that time for Italian population. They concluded that revision of normal limits for ALT is advisable. Our study also supports revision of current limits of normal. Recent research is suggesting that ALT levels above 20 IU/L are significantly associated with the risk of death from liver disease[5]. This value of 20 IU/L is almost half of the values previously accepted as acceptable values of the upper limit of normal ALT[13].

Lee JK from Korea, in 2009, worked out healthy upper limits for serum ALT in Asian populations with normal liver histology[14]. They found out that healthy ALT levels were 33 IU/L for men. Median age was 25 years for men with a median BMI of 22.3 kg/m2 in men. They concluded that the healthy ALT thresholds in biopsy-proven normal Asians were clearly lower than presently considered normal values[14]. Likewise, our study also favours lowering the current threshold of normal serum ALT.

Yagura M et al. in re-evaluation of the serum ALT upper normal limit in chronic hepatitis C patients, proposed that a suitable ULN of serum AST is <25 IU/L and ALT is <20 IU/L in chronic Hep C patients[15]. Researchers like Calvaruso V are suggesting a search for alternative noninvasive markers of liver damage[16]. They suggested that CLD, in most of the cases is asymptomatic until its terminal stages and also significant hepatic necrosis and fibrosis may be present in persistently normal ALT levels in many of the patients of HBV, HCV carriers and in patients with nonalcoholic fatty liver disease. Because large number of patients of liver diseases have a normal ALT and AST levels therefore more research should be focused to find out alternative noninvasive markers of liver damage.

CONCLUSION

Mean serum alanine aminotransferase (ALT) values observed in young healthy Pakistani adults is 29.9± 8 IU/L, which is lower than normal reference provided at present. However because of small sample size this research is not sufficient to suggest a new ULN for ALT in Pakistani population and more research work is required to ascertain ULN for ALT in our population. Moreover stastistical analysis revealed that ALT is not significantly influenced by age and BMI.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

REFERENCES

1. Neuschwander-Tetri BA, Unalp A, Creer MH. Influence of Local Reference Populations on Upper Limits of Normal for Serum Alanine Aminotransferase Levels. Arch Intern Med 2008; 168 (6), 663-6.
2. Prati D, Taioli E, Zanella A, Della Torre E, Butelli S, Del Vecchio E, et al. Updated definitions of healthy ranges for serum alanine aminotransferase levels. Ann Intern Med. 2002;137:1–9.
3. Park HN, Sinn DH, Gwak GY, Kim JE, Rhee SY, Eo SJ, et al. Upper normal threshold of serum alanine aminotransferase in identifying individuals at risk for chronic liver disease. Liver Int. 2012; 32(6): 937-44.

4. Bilal M, Tariq A, Khan S, Quratulain, Tariq A, Shahid MF, et al. Influence of gender, BMI, and ethnicity on serum ALT levels of healthy students of a medical school. J Ayub Med Coll Abbottabad. 2011; 23(1): 70-2.
5. Kim HC, Nam CM, Jee SH, Han KH, Oh DK, Suh I. Normal serum aminotransferase concentration and risk of mortality from liver diseases: prospective cohort study. BMJ. 2004; 328: 983–8.
6. Kyrlagkitsis I, Portmann B, Smith H, O'Grady J, Cramp ME. Liver histology and progression of fibrosis in individuals with chronic hepatitis C and normal elevated ALT. Am J Gastroenterol 2003; 98: 1588-93.
7. Pratt DS, Kaplan MM. Evaluation of abnormal liver-enzyme results in asymptomatic patients. N Engl J Med 2000; 342: 1266-71.
8. Kaplan MM. Alanine transferase levels: what's normal. Ann Intern Med 2002; 137: 49-50.
9. Canalias F, Camprubi S, Sanchez M, Gella FJ. Metrological traceability of values for catalytic concentration of enzymes assigned to a calibration material. Clin Chem Lab Med. 2006; 44(3): 333-9.
10. PetitClerc C, Wilding P. The theory of reference values: part 2, selection of individuals for the production of reference values. J Clin Chem Clin Biochem. 1984; 22(2): 203-8.
11. Dutta A, Saha C, Johnson CS, Chalasani N. Variability in the upper limit of normal for serum alanine aminotransferase levels: a statewide study. Hepatology. 2009; 50(6): 1957-62.
12. Leclercq I, Horsmans Y, De Bruyere M,Geubel AP. Influence of body mass index, sex and age on serum alanine aminotransferase (ALT) level in healthy blood donors. Acta Gastroenterol Belg. 1999; 62(1): 16-20.
13. Sarin SK, Kumar M. Should chronic HBV infected patients with normal ALT treated: debate. Hepatol Int. 2008; 2: 179–84.
14. Lee JK, Shim JH, Kim KM, Lim YS, Chung YH, Lee YS, et al. Estimation of the healthy upper limits for serum alanine aminotransferase in Asian populations with normal liver histology. Hepatology. 2010; 51 (5): 1577–83.
15. Yagura M,Tanaka A, Kamitsukasa H, Otsuka H, Kanno S,Aoyama T. Re-evaluation of the serum alanine aminotransferase upper normal limit in chronic hepatitis C patients. Intern Med. 2010; 49(6): 525-8.
16. Calvaruso V, Craxi A. Implication of normal liver enzymes in liver disease. J Viral Hepat. 2009; 16(8): 529-36.