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Upper Limit of Normal Serum Alanine Transaminase ALT and Correlation with Gender and BMI

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1. Abstract

Alanine transaminase ALT is considered the most specific marker for hepatocellular membrane damage, once asymptomatic ALT elevation may be the only indicator of some liver diseases such as non-alcoholic fatty liver disease NAFLD which is the most common liver disease in the western world, so it is necessary to define upper limit of normal ULN of ALT accurately to differentiate healthy and asymptomatic patients, many studies were made to evaluate ULN of ALT in different countries, all of which recommended that ULN of ALT should be lower than current reference values with presence of difference between males and females.

2. Introduction

Alanine transaminase ALT is considered the most specific marker for hepatocellular membrane damage, once asymptomatic ALT elevation may be the only indicator of some liver diseases such as non-alcoholic fatty liver disease NAFLD which is the most common liver disease in the western world, so it is necessary to define upper limit of normal ULN of ALT accurately to differentiate healthy and asymptomatic patients.

ULN of ALT is defined as mean ± standard deviation of ALT value for the healthy group [1], it has been considered at the value 40 IU / L since the 1950s, this value was determined based on population-based studies of blood donors prior to the availability of hepatitis C serological tests and before recognition of the widespread prevalence of NAFLD [2], so screen tests were done based on this value resulted omission of many patients with chronic liver disease, as ALT was considered as normal in more than half of NAFLD patients, also several studies showed presence of significant liver damage on liver biopsy in a section of patients of chronic hepatitis C with normal value of ALT [3], subsequently several studies were made to evaluate ULN of ALT in different countries and concluded the following results [4-7] (Figure 1).

Many studies have examined the relationship between ALT level with BMI and components of metabolic syndrome, such Prati study which demonstrated that BMI, dyslipidemia and carbohydrate metabolism are independently influencing factors for ALT elevation [8], while the Iranian study showed correlation between ALT level and hyperlipidemia in both sexes [6], also the Japanese study demonstrated that fatty liver has the greatest effect on ALT level followed by hypertriglyceridemia and BMI [7], the people with higher level of ALT were at greater risk for metabolic syndrome.

3. Method

Our study had been designed as cross sectional in Al-Moassat University Hospital, Damascus, Syria, from August 2013 to July 2014, the sample included 500 apparently healthy people (325 men, 175 women), a detailed history was taken and an accurate clinical examination was done to exclude the ones whom didn't meet the criteria, they were tested for Fasting Blood Sugar (FBS), Triglycerides (TG), Total Cholesterol (TC) and High Density Lipoprotein (HDL), we excluded the ones whom had one of the following values by mg/dl: FBS ≥100, TG ≥150, TC ≥220 and HDL <40, BMI was calculated by: weight (kg) / square height (m2) and the sample was divided into two groups: ones with normal BMI (< 25) and ones with elevated BMI (≥25), ALT was measured by standard method estimated in (IU/L) in Al-Moassat University Hospital laboratory, the individuals

had been excluded if they had any of the following: history of alcoholism, personal or family history of liver diseases, history of chronic systemic diseases (HTN, DM, renal failure, cardiomyopathy …), history of taking medications during the past two months including analgesics and over-the-counter drugs, history of blood transfusion or multiple sexual partners, presence of a tattoo and blood sugar disorder or dyslipidemia.

The statistical study was conducted using T Student study of independent samples to study the significance of differences between the mean of two digital variables (example study of differences between the mean ages of the sample by gender), and the categorical variables were compared using the Mann Whitney test and P-Value was considered statistically significant if is less than 0.05.

4. Results

The study group included 325 males with average age (51.84 +/- 12.521) year and 175 females with average age (49.57+/- 13.072) year, mean value of ALT was (22.45+/- 17.591) in male group, and (16.22+/-5.526) in female group.

233 males out of 325 (71.7%) and 116 females out of 175 (66.3%) had normal BMI, ALT levels followed abnormal distribution in both the male and female group, mean ALT was (19.40+/-4.804) within males and (14.40+/-4.92) within females.

The male group with elevated BMI included 92 (28.3% of total males) and mean ALT in it was (30.17+/-10.965) which is significantly higher than value in the male group with normal BMI (P<0.001), on the other side the female group with elevated BMI included 59 (33.7% of total females) and mean ALT was (19.80+/-4.895) which is also higher than value in the female group with normal BMI (P<0.001).

5. Discussion

As the level of ALT showed abnormal distribution in both the male and female group with normal BMI as well as those with elevated BMI, so the statistically higher cut-off value can be considered as ULN for ALT, consequently ULN of ALT was considered at 90% percent in both male and female group with normal BMI [9] which was equal 29 in male and 19 in female, this difference in ALT level between males and females may be explained by the difference in BMI, as mean of BMI in males and females was (23.6 ± 3) and (21.18 ± 3.3) respectively, while mean of BMI in the males and females with normal BMI was (21.2 ± 1.8) and (20.3 ± 1.99) respectively, another possible reason for this difference is that NAFLD is more associated with central obesity which is more common in males.

BMI had a statistically significant effect on ALT levels in both sexes, statistical analysis showed a direct but non-linear correlation between ALT and BMI values, it should be noted the effect of BMI on ALT level is independent of the elements of metabolic syndrome, as the study excluded people with blood glucose impairment, dyslipidemia and arterial hypertension, so elevated BMI could be considered an independent factor for ALT elevation (Figure 2-7).

Table 1: shows studies was made to evaluate ULN of ALT

Country of study	Male IU / L	Female IU / L
United States of America	29	22
Korea	31	23
Iran	21	19
Japan	29	23

Table 2: shows mean, standard deviation and T-test for comparing average age according to gender, notice P-value=0.058 which is higher than (α=0.05), so there is no statistically significant differences between the ages of the sample members according to gender

	gender	N	Mean	Std. Deviation	P-Value
Age in years	male	325	51.84	12.521	0.058 > 0.05
	female	175	49.57	13.072	

Table 3: shows mean, standard deviation and T-test for comparing mean ALT according to gender, notice P-value is less than (α=0.05), so there is statistically significant differences in mean ALT according to gender

	gender	N	Mean	Std. Deviation	P-Value
ALT	male	325	22.45	17.591	0.0001<0.05
	female	175	16.22	5.526	

Table 4: shows mean, standard deviation and T-test for comparing mean ALT in ones with normal BMI according to gender, notice P-value is less than (α=0.05), so there is statistically significant differences in mean ALT in individuals with normal BMI according to gender

	Gender	N	Mean	Std. Deviation	P-Value
ALT in individuals with normal BMI	male	233	19.4	4.804	0.0001 < 0.05
	female	116	14.4	4.92	

Table 5: shows mean, standard deviation and T-test for comparing mean ALT in ones with elevated BMI according to gender, notice P-value is less than (α=0.05), so there is statistically significant differences in mean ALT in individuals with elevated BMI according to gender

	gender	N	Mean	Std. Deviation	P-Value
ALT in individuals with elevated BMI	male	92	30.17	10.965	0.012 < 0.05
	female	59	19.8	4.895	

Table 6: shows correlation between ALT and BMI in whole sample population, Pearson correlation coefficient between the two variables (R=0.535) which is moderately-linear correlation coefficient

		BMI	ALT
BMI	Pearson Correlation	1	.535**
	Sig. (2-tailed)		.0001 < 0.05
	N	500	500
ALT	Pearson Correlation	.535**	1
	Sig. (2-tailed)	0.0001	
	N	500	500

Table 7: shows the natural distribution curve of ALT levels with the total sample population

Percentiles ALT								
BMI classes	gender	5%	10 %	25 %	50 %	75 %	90 %	95 %
Normal	male	14	15	17	17	23	29	31
	female	11	11	12	13	16	19	20
elevated	male	14	16	23	24	26	30	36
	female	12	16	16	18	20	24	25

6. Conclusion

ULN of ALT is less than the current reference value and it is different between males and females (29 IU / L in males and 19 IU / L in females), also it is affected by the BMI where there is a nonlinear direct correlation between them in both sexes and this The effect of BMI on ALT values is independent of elements of metabolic syndrome.

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