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

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Abstract

Alanine transaminase ALT and aspartate transaminase AST are considered as important marker for hepatocellular membrane damage, ALT is more specific to hepatocellular injury than AST, once transaminases rise by 1-4% of the general population; it is classified according to upper limit of normal ULN to Mild when rise up to (2-3) times of ULN such as in celiac disease, thyroid disease (hypo or hyperthyroidism), adrenal insufficiency, systemic infections, etc. Moderate when rise from 2-3 times to 20 times of ULN such as in the early stages of viral hepatitis, congestive hepatopathy and non- alcoholic fatty live disease NAFLD that accounts the most common cause of mild to moderate elevation ALT in asymptomatic patients. Severe when rise more than 20 times of UNL such as in acute viral hepatitis, ischemic hepatitis and drug induced hepatitis.

Keywords: Hyperthyroidism; Hepatitis; Asymptomatic patients

Introduction

Asymptomatic ALT elevation may be the only indicator of some liver diseases such as NAFLD, so it is necessary to define ULN accurately to differentiate healthy and asymptomatic patients. ULN of ALT is defined as mean ± standard deviation of ALT values for the healthy group, it has been considered at the value 40 IU / L since the 1950s with minor changes between laboratories depending on the used kits, 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, 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.

Methodology

Serum alanine transaminase ALT

Subsequently several 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.

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 1: Study of male and female IU/L.

This important difference in ALT values between the sexes is explained in several reasons including:

- BMI in males is greater than in females

- NAFLD is more associated with central obesity and increased waist- to-hip ratio WHR that is more common in males, so the liver is exposed to large amounts of harmful fatty acids of visceral adipose tissue.

Many studies had examined the relationship of ALT level with body mass index BMI and components of metabolic syndrome, and the most revealed correlation, Prati study demonstrated that BMI, dyslipidemia and carbohydrate metabolism are independently influencing factors for ALT elevation, a Pakistani study showed strong correlation between ALT level and BMI, where it was observed that the mean value of ALT in people with elevated BMI was 52% higher than the mean value of ALT in people with normal BMI, also an Iranian study showed correlation between ALT level and hyperlipidemia in both sexes, while ALT level was associated with BMI and waist circumference in males only, where as a Japanese study demonstrated that fatty liver has the greatest effect on ALT level followed by triglyceridemia and BMI, also it was observed that there is correlation between ALT level and development of metabolic syndrome in the long term in people who mainly did not have it, since people with higher level of ALT were at greater risk for metabolic syndrome.

Our study had been designed as cross sectional in Al-Moasat University Hospital, Damascus, Syria, from August 2013 to July 2014, with the aim to detect ULN of ALT in apparently healthy people and correlation with gender and BMI and compare the results with ones of other similar studies.

the study sample included 500 apparently healthy people (325 men, 175 women), they were informed of the purpose and content of the study and written informed consent was obtained, thorough history was taken and accurate clinical examination was done to exclude the individuals whom didn't meet the criteria, a blood sample was drawn from all the individuals after 12-hour fasting and they were tested for fasting blood sugar (FBS), triglycerides (TG), total cholesterol (TC) and high density lipoprotein (HDL), the individuals whom have blood sugar disorder or dyslipidemia were excluded according to the following values: FBS is greater or equal to 100 mg/dl, TG is greater or equal to 150 mg/dl, TC is greater or equal to 220 mg/dl and HDL is less than 40 mg/dl, the information regarding gender and age had been taken and the height and weight were measured for all the individuals by hospital clothing (hospital gown) without wearing shoes or clothes, BMI had been calculated by the following equation: weight (kg) / square height (m 2) and we approved the normal range according to WHO as (24.9-18.5 kg / m 2), the individuals were divided according to BMI value into two groups:

- Individuals with normal BMI (less than 25 kg / m2)
- Individuals with high BMI (greater than or equal to 25 kg / m2

Serum ALT was measured by standard method at a temperature of 37 ° C and estimated in international units / liter (IU/L) in Al-Moasat University Hospital laboratory exclusively to avoid possible differences if it was performed in more than one laboratory.

Results

Inclusion

Apparently healthy individuals between the ages of (18-64) years whom are volunteers from the medical and nursing staff and employees in Al-Moasat University Hospital.

Exclusion

The individuals had been excluded if they had one or more of the following:

History of alcoholism regardless the quantity or duration. Personal or family history of liver disease. History of chronic systemic diseases (for example: arterial hypertension, DM, thyroid disease, renal failure, cardiomyopathy). Use of 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 or possible signs of hepatitis by clinical examination. Blood sugar disorder or dyslipidemia.

Statistical study

The statistical study was conducted using:

Cross Tables. Mean and the standard deviation of the numerical variables. 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. P-Value is statistically significant if less than 0.05.

Describing the sample according to the patient's age in years.

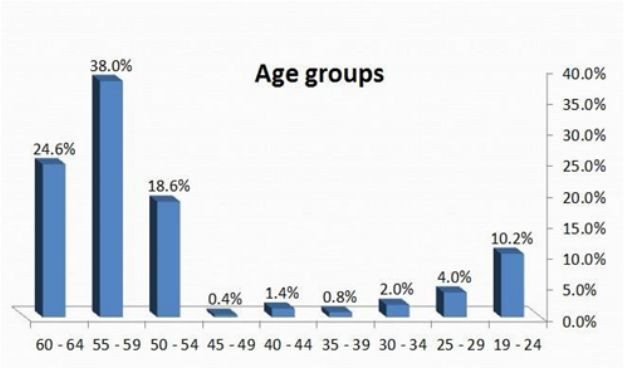

Figure 1: Patient's age in years.

Description the sample according to the categories of BMI

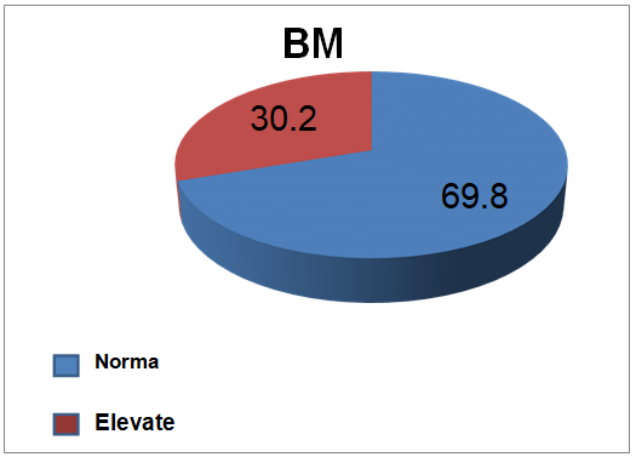

Figure 2: Categories of BMI.

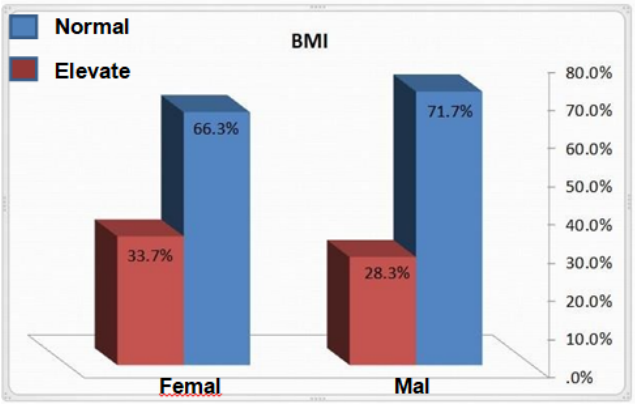

Figure 3: BMI of normal and elevate for female and male.

Study ALT

ALT in	Categories BMI	N	Mean	Std. Deviation	P-Value
male group	normal	233	19.4	4.804	0.0001 < 0.05

	elevated	92	30.17	10.965	

Table 2: ALT in male group.

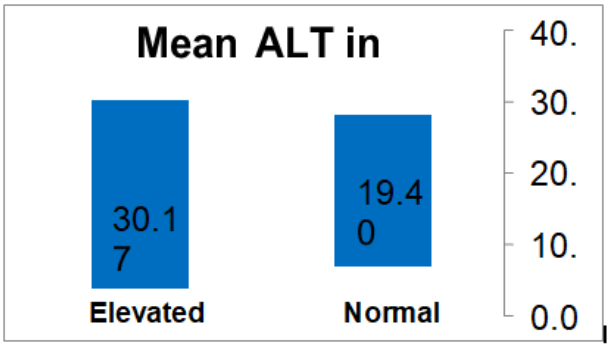

Figure 4: Comparison of ALT in the male group according to BMI categories.

ALT	Categories BMI	N	Mean	Std. Deviation	P-Value
In female group	normal	116	14.4	4.92	0.0001 < 0.05
	elevated	59	19.8	4.895	

Table 3: ALT in female group.

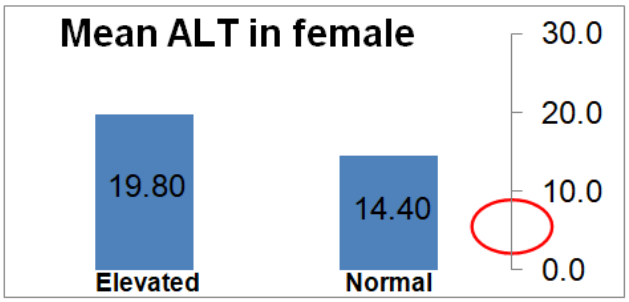

Figure 5: Comparison of ALT in the female group according to BMI categories.

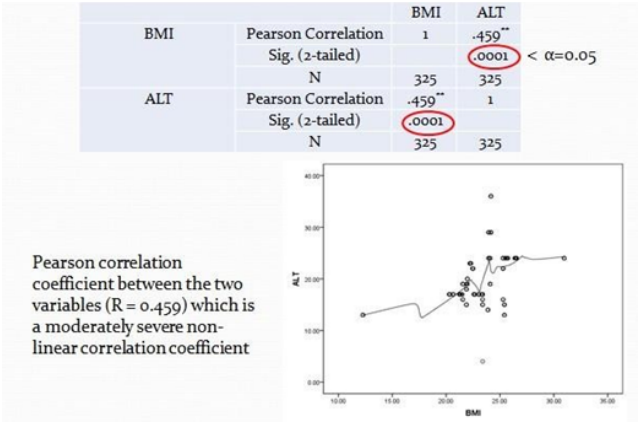

Figure 6: Study of correlation between ALT and BMI among the male group.

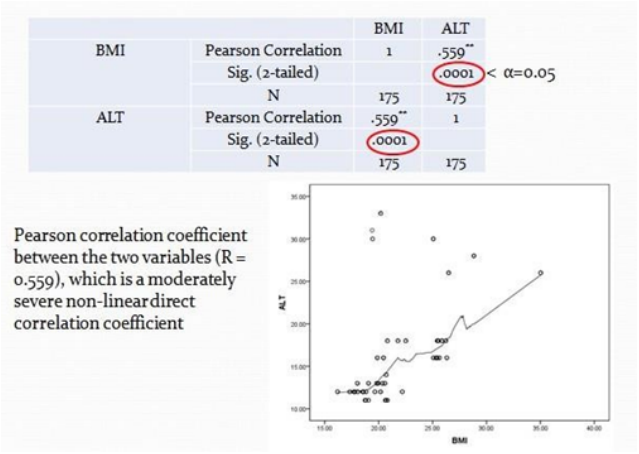

Figure 7: Study of correlation between ALT and BMI among the female group.

Discussion

The difference in ALT levels between the sexes in our study may be due to the difference in BMI values between them, the mean of BMI in the male group (23.6 ± 3) kg / m2, and in the female group (21.18 ± 3.3), the mean of BMI in the group of males with normal BMI (21.2 ± 1.8), and in the group of females with normal BMI (20.3 ± 1.99).

The difference in ALT levels between the sexes may be because NAFLD is more associated with central obesity that is more common in males.

BMI has a statistically significant effect on ALT levels in both sexes, where the mean of ALT in the male and female group with elevated BMI was higher than in the male and female group with normal BMI respectively, statistical analysis showed a direct but non-linear correlation between ALT and BMI values for both males and females.

The effect of BMI on ALT levels is independent of the elements of metabolic syndrome, because the study excluded people with blood glucose impairment, dyslipidemia and arterial hypertension, so elevated BMI could be considered an independent factor for ALT elevation.

We consider definition of ULN for ALT as the highest 90% percentile in healthy subjects with normal BMI because ALT values were of abnormal distribution in the overall study group and the group of individuals with normal BMI, the ULN for ALT should be sufficiently sensitive for scanning tests and so the use of the highest 90% percentage value is more appropriate, according to this definition, ULN of ALT is 29 IU / l in males and 19 IU / l in females, despite careful and appropriate selection of study individuals, both the total study groups and individuals with normal BMI included individuals with marginal or statistically significant values (off-line) and these individuals could be overlooked by excluding statically significant findings.

The results of this study are largely consistent with the studies previously conducted, when compared to the Prati study, we find a large convergence in the results, despite the difference in the average age of the population between the two studies (10 ±

30) years in the Parti study, while in our study (12.521 ± 51.84) years in males and (13.072 ± 49.57) years for females

Prati study demonstrated that BMI is an independent factor influencing ALT in both sexes, which is what our study also found.

There is some differences between the results of our study and the results of Korean and Japanese studies, where the ULN of ALT in them was slightly higher than the values in our study, this difference can be explained by the difference of ethnic groups between the two studies and the difference in the normal field of BMI in Asians from the field approved in our study, the Japanese study demonstrated a significant effect of BMI on ALT levels in both sexes independently of the elements of metabolic syndrome, which was also found in our study.

While we find important differences when comparing the results of our study with the results of Iranian study, which showed a correlation between the values of ALT and BMI in males only, but the Iranian study was conducted on the elderly category (greater than 50 years).

There are also important differences between the results of our study and the results of Pakistani study, where the mean ALT in the Pakistani study was 32.1 IU / l in males and

22.6 IU / l in females, while in our study (22.45 in males and 16.22 in females), however, the Pakistani study A small sample size (143) was performed and did not evaluate other factors that may affect ALT levels such as high blood sugar and dyslipidemia.

Study limitations

The possibility of asymptomatic individuals with latent hepatitis such as autoimmune hepatitis or primary biliary cirrhosis or asymptomatic hepatotoxicity within the study group, but this point may be overlooked due to the scarcity of these lesions and the tightening of inclusion and exclusion criteria, also alcoholic evaluation is based on history only, which may cause a misleading rise in ALT values due to alcoholism due to individuals' denial of the story of alcohol abuse, the other limitation is that no tests were performed to clear chronic viral hepatitis (HBsAg and AntiHCV) when selecting the study sample, except that people with potential risk factors for chronic viral hepatitis (history of blood transfusions, tattoo, or multiple sexual partners) were excluded in addition to the large sample size and statistical analysis used What excluded marginal or excluding values makes the effect of this point on the study results insignificant.

Conclusion

Upper limit of normal for ALT is less than the current reference values and it differs between males and females (29 IU / L in males and 19 IU / L in females) and 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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