Influence of body mass index, sex and age on serum alanine aminotransferase (ALT) level in healthy blood donors

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Abstract

Background and aim **: Serum alanine aminotransferase (ALT) level is the most common screening test as part of a routine evaluation of liver damage. In order to determine the factors influencing this liver function test in normal subjects, the relationship between ALT level and gender, age and body mass index (BMI) was studied in a large population of healthy blood donors.**

Methods **: This population included 9,420 volunteer blood donors (4,488 men and 4,932 women aged from 18 to 70 years) selected on the basis of negative answers to a detailed medical questionnaire including past medical history, drug and alcohol consumption, on the absence of clinical signs of liver disease, on the negativity of serological testing for hepatitis B and C virus and HIV.**

Results **: In the overall population, the mean serum ALT value was 21.8 I.U./L and the mean BMI was 24.4 kg/m^2. There was a positive significant correlation between serum ALT level and BMI (Pearson $r = 0.54$; $p < 0.001$) and between ALT and age (Pearson $r = 0.25$; $p < 0.001$).**

A major sex-difference in ALT value was observed, the mean ALT value being higher in men than in women (26.8 ± 13.6 vs. 17.2 ± 8.1 I.U./L, $p < 0.0001$). In both sexes, ALT level was significantly correlated with BMI (Pearson $r = 0.45$ in men and $r = 0.37$ in women ; $p < 0.001$). In women a consistent rise in BMI and ALT value with increasing age was observed whereas in men BMI and ALT level only increased with age up to the fifth decade.

In conclusion**, there was a significant positive correlation between ALT and BMI regardless the gender in a population of healthy volunteer blood donors. Moreover, at the same age and the same BMI, ALT was significantly lower in women than in men suggesting that the normal range for ALT value should be adjusted for gender. So gender and BMI have to be considered in the interpretation of ALT values.** (Acta gastroenterol. belg., **1999**, 62, **16-20**).

Key words : alanine aminotransferase, blood donors, obesity, gender, age.

Introduction

Measuring serum alanine aminotransferase (ALT) level is the most frequently used screening test as part of a routine evaluation of liver damage. It is generally accepted that serum ALT level reflects the severity of liver damage in acute liver disease but its value for assessing the severity in chronic liver disease is more doubtful (1). On the contrary, elevated ALT values have been found in healthy subjects (2). This liver function test is also used by blood banks as a criteria to accept or refuse blood donation. The current recommendations of the American Association of Blood Banks for deferring blood donors are two different serum levels of ALT that are more than 2 standard deviations (SD) above the established mean value of ALT or a single ALT level that is more than two times the upper limit of normal (3). However, until now, in clinical research, the definition of the upper limit of normal is never detailed. In our laboratory, the normal value for ALT is based on ALT determination in 200 healthy subjects (mean : 14.8 I.U./L, SD : 8.4, normal range : 6-32 I.U./L) and this undependently of demographical factors such as sex, age, race and BMI.

In order to determine the influence of age, gender and BMI on this function test, we have analyzed the relationship between ALT level and such factors in a large population of 9,420 healthy blood donors.

Material and methods

1. *Study population - Blood donors*

The study population included 12,000 consecutive blood donors seen from January 1995 to December 1996 at the UCL - Red cross blood transfusion center (Brussels, Belgium). Prior to blood donation, each volunteer blood donor was asked to answer a detailed medical questionnaire inspired by that from the American Association for Blood Banks (4). This questionnaire included past personal medical history, familial medical background, use of drug and alcohol consumption. Each subject was submitted to a physical examination. Age, height and weight were recorded and the body mass index (BMI) was calculated as the ratio of body weight (kg)/height (m^2). On a routine basis, all subjects underwent haemoglobin level, total blood cells count, sedimentation speed of red blood cells, Hbs Ag, Hbc Ab (Abbott Laboratories, North Chicago IL, USA), HCV Ab (HCV-100, Elisa test, Ortho Diagnostics, Ratinan NJ, USA), and HIV determinations as well as ALT (using the BM-GPT (HiCo) ; BM/Hitachi 917 ; Boehringer Mannheim Diagnostics, Mannheim, Germany).

Subjects completed a negative medical enquiry, a normal physical examination, a normal haemoglobin blood level, a normal blood cell count and the absence of inflammatory syndrome (normal blood cell count and normal sedimentation speed of the red blood cells) were considered for this study. Of these 12,000 subjects,

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2,580 were excluded on the basis of incomplete morphometrical data or because of positive or undetermined viral serology, including HBV, HCV and HIV. The study group thus included 9,420 volunteer blood donors (4,488 males and 4,932 females).

In our laboratory, normal values for serum ALT determined for 200 healthy subjects, independently of sex and age, are 6 to 32 I.U./L (mean ± 2 SD). In our center, positive answer to the detailed medical questionnaire, positivity for one or more viral serological tests and/or ALT level higher than 32 I.U./L (mean + 2 SD) were considered as criteria to discard blood for transfusion (3).

2. *Statistical analysis*

Student' *t*-test for unpaired variables was used for comparison between groups. Pearson correlation coefficient (Pearson r) was applied to data to determine the correlation between variables. The statistical significance level in this study was $p \leq 0.05$.

Results

In the overall population, the mean serum ALT value was 21.8 I.U./L (range 5-79). The mean BMI was 24.4 kg/m² (range 17-40). The mean age of subjects was 37.7 years (range 18-71). The distribution of ALT, age and BMI in the population studied is shown in Fig. 1. There was a statistically significant positive correlation between serum ALT level and BMI (Pearson r = 0.54 ; $p < 0.001$) and between ALT and age (Pearson r = 0.25 ; $p < 0.001$).

In the 4,488 men, mean ALT value was 26.84 I.U./L (range 5-79), the mean BMI being 24.9 kg/m² (range 17-40) and, the mean age 38.8 years (range 18.3-71). ALT values were significantly correlated with BMI (Pearson r = 0.45 ; $p < 0.001$) (Fig. 2) and were increased with age up to the fifth decade (table I).

In the 4,932 women, mean ALT values was 17.2 I.U./L (range 5-79), mean BMI 23.4 kg/m² (range 17-40) and mean age 36.8 years (range 18.2-70.7). ALT values were also significantly correlated with BMI

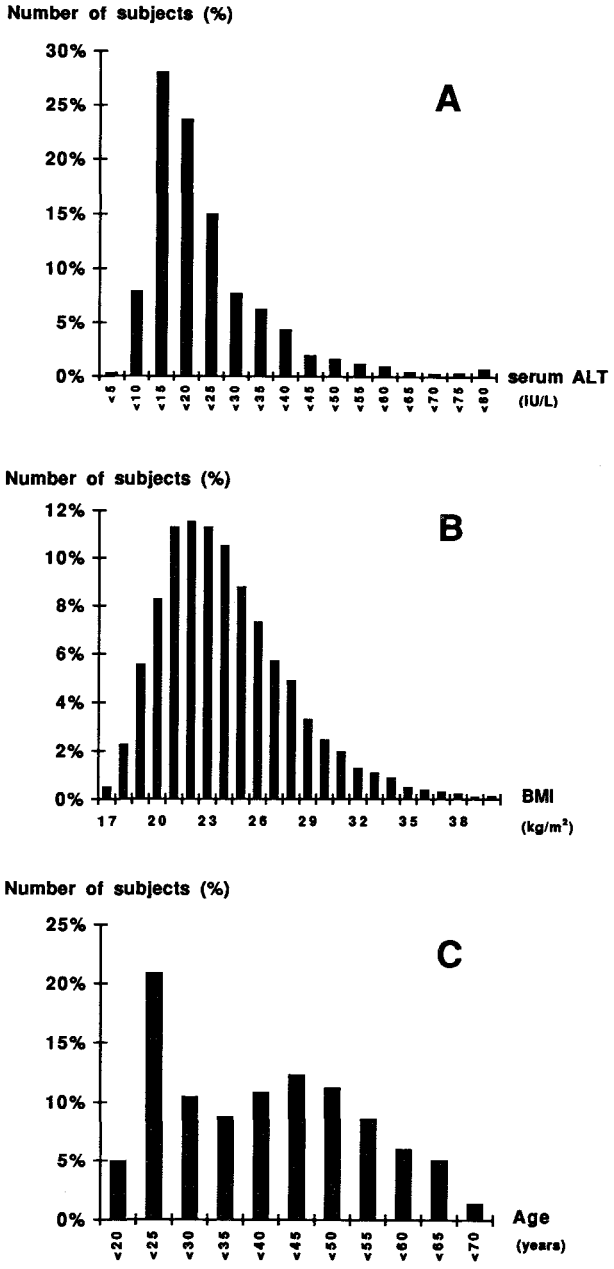

Fig. 1. — Distribution of ALT (A), BMI (B), and age (C) in 9,420 healthy volunteer blood donors.

Table I. — **Effects of age and sex on BMI and ALT values**

Age years	Women N = 4,932			Men N = 4,488		
	n	BMI kg/m²	ALT I.U./L	n	BMI kg/m²	ALT I.U./L
18-20	297	21.6 ± 2.9*	15.0 ± 6.4*	169	21.8 ± 2.3*	17.7 ± 7.5*
20-25	1167	21.7 ± 2.9	16.1 ± 7.9	797	22.8 ± 3.0	22.5 ± 11.8
25-30	491	22.5 ± 3.5	16.7 ± 8.3	490	23.8 ± 3.3	25.5 ± 15.5
30-35	395	23.2 ± 3.8	15.7 ± 6.7	426	24.8 ± 3.3	27.1 ± 14.1
35-40	525	23.6 ± 3.8	16.8 ± 6.9	494	25.1 ± 3.5	28.7 ± 14.3
40-45	586	24.1 ± 4.4	17.8 ± 9.2	569	25.7 ± 3.6	29.7 ± 14.4
45-50	516	24.3 ± 3.9	17.9 ± 7.1	540	26.2 ± 3.8	30.8 ± 14.6
50-55	399	25.0 ± 4.2	19.2 ± 9.3	407	26.7 ± 3.5	29.2 ± 13.1
55-60	278	25.6 ± 4.3	20.0 ± 9.2	282	26.7 ± 3.5	28.2 ± 12.1
60-70	278	25.7 ± 3.9	20.3 ± 7.8	314	26.3 ± 3.1	25.2 ± 10.5

* mean values ± standard deviation.

(Pearson r = 0.37 ; $p < 0.001$) (Fig. 2), moreover, a consistent rise in BMI and ALT level with increasing age was observed (Table I).

When examined using the *t*-test for unlinked random samples, the ALT values were found significantly lower in females than in males (17.2 ± 8.1 versus 26.8 ± 13.55 I.U./L ; $p < 0.0001$). BMI was also significantly lower in females (23.36 ± 3.94 versus 24.93 ± 3.68 kg/m^2, $p < 0.0001$) ; the frequency of distribution of BMI was quite different between the two genders, being in the normal range (< 25 kg/m^2) in 76.9% of women and in 61.7% of men (Fig. 3). The sex ratio is 1:1 in all range of age excepted in the group of subjects under 25 years in whitch the sex ratio M:F is 1:1.5) (Table I).

At the same BMI and whatever the BMI, ALT levels were significantly lower in women than in men (Fig. 2). At the same age, the mean ALT level and the mean BMI were also lower in women than in men (Table I).

Five percent of female and 24.9% of male subjects had above-normal serum ALT level. In both sexes, in this group of subjects with above-normal ALT values, ALT level was positively related to BMI ($p < 0.001$).

Discussion

In this study 9,420 adult volunteer blood donors were selected on the basis of negative answers to a detailed medical questionnaire and on the negativity of sero-

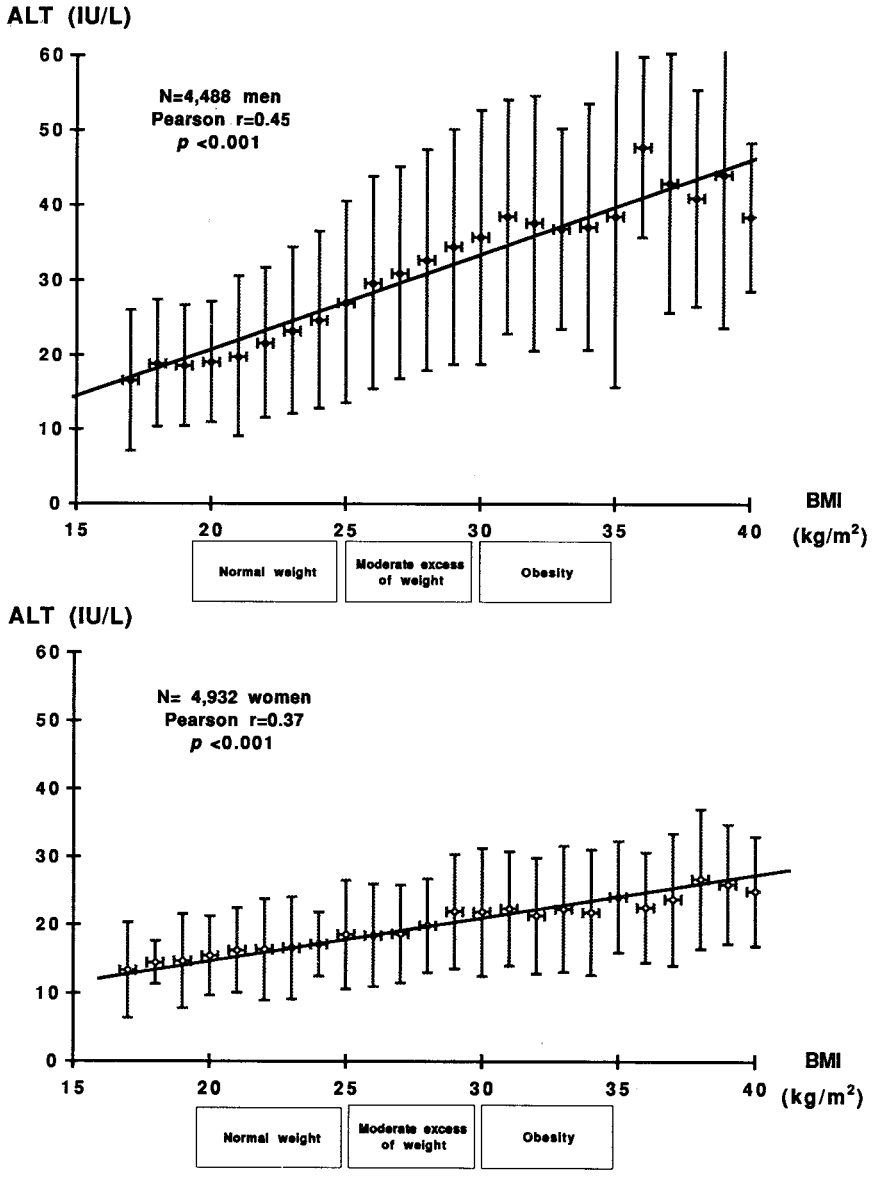

Fig. 2. — Variation of ALT values with BMI in 4,488 male (A plain symbol) and 4,932 female (B open symbol) healthy volunteer blood donors. Mean ALT and mean BMI values ± SD for each unit of BMI. Non parametrical coefficient of correlation (Pearson r) calculated on the overall group with regression line (continuous line) (y = 11.852 + 1.552 × in men and y = 4.062 + 0.563 × in women).

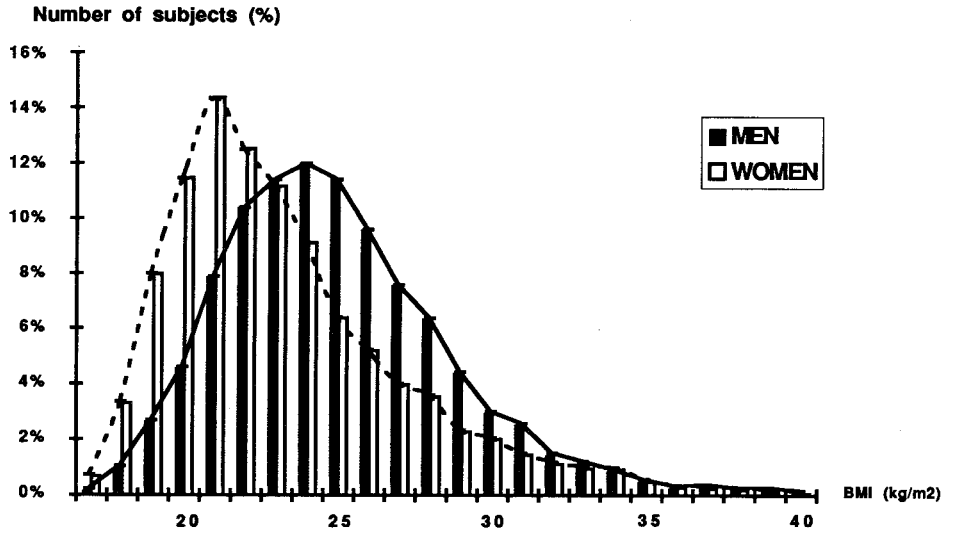

Fig. 3. — Distribution of BMI (kg/m^2) in 4,488 male (plain bar) and 4,932 female (open bar) healthy volunteer blood donors. Normal weight : BMI between 20-25 kg/m^2, **Moderate excess of weight** : BMI between 25-30 kg/m^2, **Obesity** : BMI between 30-35 kg/m^2, **Morbid obesity** : BMI > 35 kg/m^2.

logical testing for hepatitis B and C virus and HIV (3). In this population, composed of subjects considered to be healthy, the ALT level was 21.8 ± 11.8 I.U./L. The BMI in this selected population was lower than the BMI observed in the overall non selected Belgian population (5,6), a feature likely explained by the exclusion of unhealthy subjects and/or because the fact that in Belgium blood donation is a voluntary act which might be linked to a healthier way of life.

A statistically significant correlation between serum ALT level and BMI was shown in this population, a feature well in accordance with the known correlation between ALT level and body weight (7,8,9,10). Liver volume has also been shown to be positively correlated with body weight or body surface (11). By analogy with the CPK level which is correlated with the muscular cell mass (12), ALT value could be related in the absence of hepatocellular cell injury to liver volume and the number of hepatocytes even if, to our knowledge, this correlation between ALT and hepatocyte mass has never been investigated.

Since mildly elevated ALT is the most frequent biochemical abnormality described in fatty liver (13,14), another hypothesis is that increased ALT values could reflect fatty liver or steatohepatitis. Fatty liver changes is the most frequent feature observed on liver biopsy in more than 80% of asymptomatic patients referred for persistently raised aminotransferases after the exclusion of patients with clinical signs of liver disease and/or viral hepatitis (15). Also, in a population of healthy victims of fatal traffic accidents considered to be representative for the general population, fatty liver was observed in 21 to 24% of cases and found to be associated with a higher liver volume and a higher body weight than those observed in subjects with normal liver histology (16,17). More than 50% of subjects with a moderate excess of weight (BMI between 25 and 30 kg/m^2) and more than 90% of obese subjects (BMI > 30 kg/m^2) exhibited an hepatomegaly, a moderate elevation in serum ALT level and had fatty liver infiltration (14,18). In obese patients, weight reduction induced a decrease in liver volume and in ALT whereas weight gain is associated with an increase in ALT levels (18). Taken all together, these observations suggest that the correlation between ALT and BMI is likely related to various degree of fatty liver although it has been suggested that enzymes abnormalities have no direct correlation with fat liver content on the basis of a single biopsy examination (19). Such an hypothesis might only be confirmed in a large number of randomly selected healthy subjects with available morphometrical data, total fat liver content determination and liver histology, a material which does not exist for obvious ethical reasons.

Moreover, the close correlation between ALT and BMI is also observed in the restricted group of subjects with above-normal ALT values. This observation strengths the direct link between body weight and ALT level most likely as a consequence of liver fat changes.

Similarly to previously reported data (7-10,20), in this population, a major sex-difference in ALT values was observed, the mean ALT value being higher in men than in women. This gender difference is not explained by a higher BMI found in men in comparison to women since such difference persisted whatever the BMI considered. This suggests that this difference is related to other factors such as a higher liver volume (11). The existence of a close correlation between ATL values and BMI in both gender favours this last hypothesis.

In spite of a similar range of ages in both gender, a significant correlation between ALT and age was only apparent in women. However and only in this gender group, a significant correlation was observed between age and BMI suggesting that a progressive increase in BMI in women is the sole factor responsible for the close association observed between age and ALT. Considering the high prevalence of fatty liver in women in association with moderate overweight or high glucidic diet (14,21), the reference to a normal value for ALT not adjusted for gender could underestimate the diagnosis of liver steatosis.

In conclusion, there was a significant positive correlation between ALT and BMI in this large normal population suggesting that increased ALT values observed in subjects with high BMI could be related to various degree of liver steatosis. Moreover, whatever the BMI, ALT was significantly lower in women than in men. To estimate liver damage on the basis of ALT level and to better determine the criteria for blood donation, factors such as age, gender and BMI should thus be taken into account for interpretation of ALT values.

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