



Study of serum alanine-aminotransferase levels in blood donors in Spain

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ABSTRACT

Background and Objective. Serum alanine-aminotransferase (ALT) is being used as a surrogate test for preventing post-transfusion viral hepatitis. However, ALT elevation is influenced by many factors. We have studied ALT levels in 1,036 consecutive blood donors to determine their association with gender, obesity, and hepatitis virus infection markers.

Design and Methods. In each donation aspartate-aminotransferase (AST), lactate dehydrogenase (LDH) and γ -glutamyl transferase (γ GT) activity were also determined and body mass index (BMI) was calculated.

Results. Five hundred seventy-nine men and 457 women donated blood; ALT activity was 25.3 ± 14.5 IU/L (mean \pm SD) for men and 16.3 ± 7.9 IU/L for women ($p \leq 0.0005$). The upper normal value for men was 56 IU/L and 34 IU/L for women. On applying this value to the study group 4.8% of the men and 2% of the women had values greater than the cutoff. Among the men with increased ALT levels, 53.5% had a BMI >27 , 7.1% also had an increased level of GGT and 7.1% had increased levels of AST and LDH. None of them were HBsAg nor anti-HCV positive. Among the women with increased ALT, 33.3% had BMI >27 , 33.3% had increased levels of LDH and AST, and 11.1% were anti-HCV positive (only 1 donor).

Interpretation and Conclusions. It seems clear that different cutoff values should be considered for men and women. Factors such as obesity, may account for more than 50% of the cases with increased ALT values, indicating the low specificity of the test.

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Key words: alanine aminotransferase, blood donors, Spain, hepatitis, screening

In some countries whole blood donations are tested for alanine-aminotransferase levels (ALT) as a surrogate marker of infectious hepatitis. Thus, donors with an increased level of ALT are excluded from blood donation. However, the efficacy of ALT testing in preventing hepatitis associated to transfu-

sion has been controversial^{1,2} especially after the introduction of hepatitis C virus screening.³⁻⁵

The main reason for the lack of efficacy is that, in addition to infectious agents with liver tropism, there are other causes that may increase ALT levels such as obesity,⁶⁻⁸ alcohol intake⁹ and drugs. Moreover, there are extrahepatic sources of ALT such as the muscle,¹⁰ kidney and red blood cells¹¹ which can increase ALT levels in serum.

In Spain it is not mandatory to test whole blood donation for ALT before transfusion. However, recovered plasma from collected blood is used in the manufacturing of plasma derivatives, and Spanish and European regulations require this plasma to be tested for ALT levels. We therefore decided to establish the normal value in our population. In addition, we studied the association of factors such as gender, obesity and hepatitis virus infection markers with ALT levels in our population of blood donors.

Materials and Methods

Blood donors and methods

The study group consisted of 1,036 consecutive blood donations selected and screened according to standard Spanish regulations collected in 10 days. In each donation an extra pilot sample was withdrawn for serum separation.

In addition to serum ALT, other enzymes were quantified: aspartate-aminotransferase (AST), lactate dehydrogenase (LDH) and γ -glutamyl transferase (γ GT). Enzyme activities were determined in a Technicon DAX 72, Bayer Diagnostics analyzer according to the methods recommended by the *International Federation of Clinical Chemistry*.

Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared according to the recommendation of the *National Institute of Health Consensus Development Panel*.¹² A normal value was considered as up to 27. HBsAg and anti-HCV were measured using Ortho EIA kits (Ortho Diagnostics, Raritan, NJ, USA). Repeatedly reactive samples for second-generation anti-HCV were tested with RIBA-2 test (Ortho Diagnostics, Raritan, NJ, USA).

Statistical analysis

Statistical analysis was performed with SPSS for Windows 6.1.3 statistical software. Cutoff values for

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ALT were calculated as the fractile 0.975 of the distribution,¹³ after excluding outlier values (mean plus 3SD).¹⁴ The t-test was used to assess the significance of ALT differences between men and women.

Results

The donor group was comprised of 579 men and 457 women, aged 18 to 65 years (median 24). The mean ALT activity level for men was 25 IU/L with a standard deviation of 14.5 IU/L, while for women the figures were 16 ± 7.9 IU/L. The histograms of frequencies are shown in Figure 1. The difference observed was statistically significant ($p \leq 0.0005$).

The calculated upper normal ALT value was 56 IU/L for male blood donors and 34 IU/L for female blood donors. On applying this value to the study group, 4.8% of the men (28 blood donors) and 2% of the women (9 blood donors) were found to have serum ALT activity greater than the cutoff value. In all cases the increase was between 1 and 2 times the upper normal level. Among men with increased ALT levels 53.5% had a BMI greater than 27, 7.1% also had increased levels of AST-LDH and 7.1% had increased levels of γ GT. None had markers of hepatitis B or C infection.

Among women with ALT levels higher than the cutoff value, 33.3% had a BMI greater than 27, 33.3% had increased levels of AST-LDH and 11.1% (1 donor) had antibodies against HCV. None had increased levels of γ GT.

After implementing the cutoff over one year, 130 donors with ALT levels between 1 and 2 times the cutoff value donated blood twice or more. Only 24% of these donors showed an increased ALT value in the second donation.

Discussion

Increased ALT levels are being used in some countries as a surrogate marker of infectious hepatitis. Their implementation, however, is not a trivial issue since determination of cutoff values is not standardized and factors such as the instruments used for measurement, population studied, gender, etc. may affect the results. To avoid these problems it has been suggested that individual laboratories should determine cutoff values for donor deferral.^{15,16}

In our population, mean ALT levels were significantly higher in males than in females. Therefore different cutoff values were established, being 56 IU/L for men and 34 IU/L for women. Similar figures have been found in other populations of blood donors.¹⁶ The reason for the observed difference between male and female blood donors has not been addressed in the literature, although it has been reported in other populations.^{9,16-19} Moreover, on applying these values to the study group, the percentage of blood donors with values higher than the cutoff was twice as high for men (4.8%) than for women (2%). The same is also true for other groups.^{9,16-19} This difference is probably due to a higher frequency of habits that

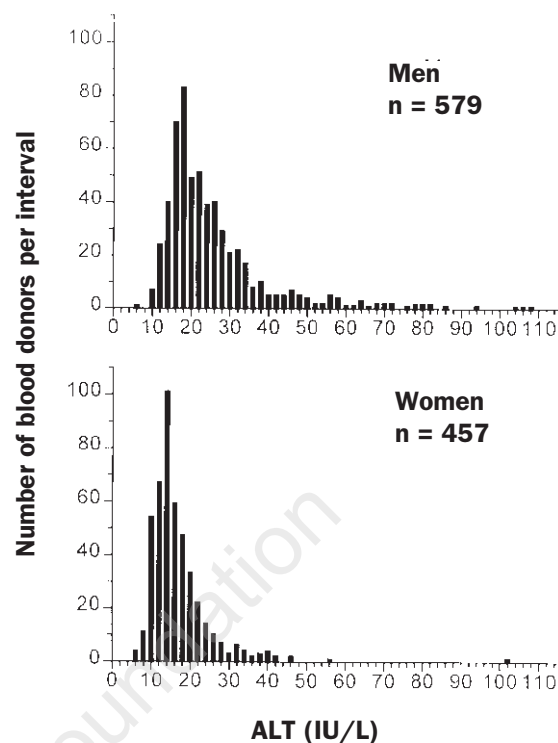


Figure 1. Histograms showing ALT levels in male (upper) and in female (lower) blood donors.

might affect ALT levels (smoking, alcohol consumption, etc.) in men than in women.²⁰

None of the male blood donors with ALT serum activity higher than the cutoff (4.8% of the population) had serologic markers of hepatitis B or C infection. Anti-HCV positivity was found in one out of 9 female blood donors with serum ALT activity greater than the cutoff value, but the small number of subjects does not allow any conclusion. Interestingly, only 24% of the blood donors with ALT values between 1 and 2 times the cutoff who donated blood the following year, had an ALT level above the cutoff value. This observation may suggest that the cause for these small increases in ALT might, in most cases, be transitory (drugs, physical exercise, etc.) although an infectious cause for these transitory increases of ALT, can obviously not be ruled out.

Although not enforced for transfusion, as long as American and European regulatory agencies require plasma devoted to plasma fractionation to be tested for ALT levels,²¹ we will be obliged to do the test in order to transfer the plasma to the fractionation industry. If this is the case, a separate cutoff for each sex seems mandatory in order not to discard blood components with slightly elevated ALT levels.

Contributions and Acknowledgments

ML, JC, RM and AO were responsible for the conception of the study, data handling and statistical analysis. JLB, NG, EM and AB were responsible of biochemical measurements. All the authors contributed to data interpretation and writing of the paper. The criteria applied to establish author order was the degree of involvement in the realization of the study.

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Disclosures

Conflict of interest: none

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References

- Klein HG. Controversies in transfusion medicine - Alanine aminotransferase screening of blood donors: Pro. *Transfusion* 1990; 30:363-7.
- Spurling CL, Saxena S. Controversies in transfusion medicine - Alanine aminotransferase screening of blood donors: Con. *Transfusion* 1990; 30:368-73.
- Blajchman MA, Bull SB, Feinman SV. Post-transfusion hepatitis: impact of non-A, non-B hepatitis surrogate tests. *Lancet* 1995; 345:21-5.
- Busch MP, Korelitz JJ, Kleinman SH, et al. Declining value of alanine aminotransferase in screening of blood donors to prevent post-transfusion hepatitis B and C virus infection. *Transfusion* 1995; 35:903-10.
- Cable R, Badon S, Pray C, Popovsky MA. Limited utility of alanine aminotransferase screening of hepatitis C antibody-screened blood donors. *Transfusion* 1997; 37:206-10.
- Hetland G, Holme I, Stromme JH. Co-variation of alanine aminotransferase levels with relative weight in blood donors. *Scand J Clin Lab Invest* 1992; 52:51-5.
- Wejstal R, Hansson G, Lindholm A, Norkrans G. Persistent alanine aminotransferase elevation in healthy Swedish blood donors - mainly caused by obesity. *Vox Sang* 1988; 55:152-6.
- Ramesh V, Saraswat S, Choudhury N, Gupta RK. Relationship of serum alanine aminotransferase (ALT) to body mass index (BMI) in blood donors: The need to correct ALT for BMI in blood donor screening. *Transfusion Med* 1995; 5:273-4.
- Bizzaro N, Tremolada F, Casarin C, et al. Serum alanine aminotransferase levels among volunteer blood donors: effect of sex, alcohol intake and obesity. *Ital J Gastroenterol* 1992; 24:237-41.
- Clement DJ, McGuire MP, Kundrotas LW, Andrzejewski A. Elevated serum alanine aminotransferase (ALT) associated with muscle injury/exercise in a healthy young blood donor population. *Am J Gastroenterol* 1992; 87:A1297.
- Moss DW, Henderson AR, Kachmar JF. Enzymes. In: Tietz NW, ed. *Textbook of Clinical Chemistry*. Philadelphia: Saunders Co., 1986. p. 619-762.
- National Institutes of Health Consensus Development Statement. Health implications of obesity. *Ann Intern Med* 1985; 103:147-51.
- Massod MF. Non parametric percentile estimate of clinical normal ranges. *Am J Med Technol* 1977; 43:243-52.
- Standard Committee of the College of American Pathologists. Guidelines for evaluating laboratory performance in survey and proficiency testing program. A report of tentative criteria used in the 1968 survey of the College of American Pathologists. *Am J Clin Pathol* 1968; 49:457-8.
- Dorizzi RM. Note on the measurement of alanine aminotransferase in the screening of blood donors. *Vox Sang* 1992; 62:246-7.
- Boudart D, Beauplet A, Muller JY. How to determine the alanine-aminotransferase threshold in blood donors. *Vox Sang* 1993; 65:159-60.
- Briere RO. Serum ALT levels. Effect of sex, race, and obesity on unit rejection rate. *Transfusion* 1988; 28:392-3.
- Anderson NAB, Raafat A, Shwe KH, et al. UK multi-centre study on blood donors for surrogate markers of non-a hepatitis non-b hepatitis. Part I: Alanine transferase and anti-HBc testing. *Transfusion Med* 1992; 2:301-10.
- Caspari G, Gerlich WH, Beyer J, Schmitt H. Non-specific and specific anti-HCV results correlated to age, sex, transaminase, rhesus blood group and follow-up in blood donors. *Arch Virol* 1997; 142:473-89.
- Whitehead TP, Robinson D, Allaway SL. The effects of cigarette smoking and alcohol consumption on serum liver enzyme activities: A dose-related study in men. *Ann Clin Biochem* 1996; 33:530-5.
- AABB. Changes to Standards. Association Bulletin #95-6 (June 27, 1995).