Accuracy of the alanine aminotransferase test in the identification of glutamic oxaloacetic hypertransaminasemia in healthy adults from Villa el Salvador, Peru

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Abstract

Introduction: The measurement of aspartate and alanine aminotransferase are used for the diagnosis and monitoring of different organic disorders. Both tests are part of the "liver profile" routinely requested in private consultations and in health campaigns.

Objective: To determine the diagnostic accuracy of glutamic oxaloacetic hypertransaminasemia by measuring alanine aminotransferase levels in healthy adults who attend preventive health evaluations.

Methodology: Analytical, retrospective, cross-sectional study and non-probabilistic sampling based on the results of 846 patients evaluated from a polyclinic in Villa el Salvador, Peru. The variables were aspartate and alanine aminotransferase. Analysis was performed using the receiver operating characteristic curve, Chi-square, Cramer's V, relative risk, and Spearman's Rho since the distribution was not normal.

Results: The area under the receiver's operating characteristic curve was 0.927 in the total for both sexes, 0.961 in women and 0.910 in men. The values suggested the cut-off point of ALT in women of 42.50 U/L (sensitivity 84%, specificity 85%), in men of 40.50 U/L (sensitivity 95%, specificity 77%) and in the total 39.50 U/L (92% sensitivity, 77% specificity). Chi-square and Cramer's V tests found a strong and positive relationship. Men with elevated ALT had 82.81 times greater risk of elevated AST than men with normal ALT, 32.53 times greater in women and 42.84 times in total.

Conclusions: In healthy adults, simultaneous measurement of alanine and aspartate aminotransferase is not essential. Being able to dispense with aspartate aminotransferase since the measurement of alanine aminotrans-

ferase has high sensitivity and specificity to detect both hypertransaminasemias from a diagnostic and economic benefit point of view.

Keywords: Alanine Transaminase; Aspartate Aminotransferases; ROC Curve; Sensitivity and Specificity; Chi-Square Distribution

Resumen

Introducción: la medición de aspartato y alanina aminotransferasa son utilizados para el diagnóstico y seguimiento de diferentes trastornos orgánicos. Ambos exámenes forman parte del perfil hepático solicitado rutinariamente en consultas privadas y en campañas de salud.

Objetivo: determinar la precisión diagnóstica de la hipertransaminasemia glutámico oxalacética por medio de la medición de los niveles de alanina aminotransferasa en adultos sanos que acuden a evaluaciones preventivas de salud.

Metodología: estudio analítico, retrospectivo, transversal y muestreo no probabilístico basado en resultados de 846 pacientes evaluados desde en un policlínico de Villa el Salvador, Perú. Las variables fueron aspartato y alanina aminotransferasa. El análisis se realizó mediante la curva de característica operativa de receptor, Chi-cuadrado, V de Cramer, riesgo relativo y Rho de Spearman ya que la distribución no fue normal.

Resultados: el área bajo la curva de característica operativa del receptor fue 0.927 en el total de ambos sexos, 0.961 en mujeres y 0.910 en hombres. Los valores sugirieron el punto de corte de ALT en mujeres de 42.50 U/L (sensibilidad 84%, especificidad 85%), en hombres de 40.50 U/L (sensibilidad 95%, especificidad 77 %) y en el total 39.50 U/L (sensibilidad 92%, especificidad 77%). Las pruebas Chi-cuadrado y V de Cramer encontraron una relación fuerte y positiva. Los hombres con ALT elevado tuvieron 82.81 veces mayor riesgo de AST elevado que los hombres con ALT normal, en mujeres, 32,53 veces mayor y en el total, 42.84.

Conclusiones: en adultos sanos, medir simultáneamente la alanina y aspartato aminotransferasa no es esencial. Desde un punto de vista de beneficio diagnóstico y económico, se puede prescindir de la aspartato aminotransferasa ya que la medición de la alanina aminotransferasa tiene alta sensibilidad y especificidad para detectar ambas hipertransaminasemias.

Palabras clave: alanina transaminasa; aspartato aminotransferasas; curva ROC; sensibilidad y especificidad; distribución de Chi-Cuadrado.

Introduction

Aminotransferases, formerly known as transaminases (1), are enzymes involved in the interaction between amino acids and oxoacids with respect to the transfer of amino groups (2). The most clinically relevant are aspartate aminotransferase (AST), previously referred to as glutamic oxaloacetic transaminase, and alanine aminotransferase (ALT), formerly called glutamic pyruvic transaminase (3).

Elevations in the concentrations of these aminotransferases are commonly considered indicative of muscle, liver, cardiac, and other types of damage (4). They are produced in the liver, which uses them for the synthesis and breakdown of amino acids for various biosynthetic pathways (5). In this regard, in the presence of liver or systemic damage, the permeability of the cell membrane increases, resulting in a greater release of these enzymes into the bloodstream (6). The tissue activity of AST, from highest to lowest, is found in the heart, liver, skeletal muscle, kidney, pancreas, spleen, lungs, and erythrocytes (7). The tissue concentration of ALT is similar, with the highest to lowest activity found in the liver, kidneys, myocardium, skeletal muscle, pancreas, spleen, lungs, and erythrocytes (8).

AST and ALT are nonspecific markers of tissue injury (9). In the past, both enzymes were measured together for the diagnosis and monitoring of myocardial infarctions, but they have since been replaced by more specific markers such as CPK-MB (10). These enzymes can also be elevated in viral infections such as mononucleosis and hepatitis A, B, and C (11), respiratory viral illnesses, alcohol consumption (12), pancreatic disorders (13), among others. Therefore, their use as the sole diagnostic tool is limited, and clinical and laboratory assessments are necessary to determine the etiology of the underlying disease (14). Exceptions can occur, such as in severe alcoholic liver disease, where AST levels can be up to three times higher than ALT levels (15).

AST and ALT are part of the group of tests known as the liver function panel, which primarily includes total, direct, and indirect bilirubin, albumin, globulins, total proteins, and alkaline phosphatase (16). This panel is widely used in public and private healthcare centers as part of preventive or follow-up evaluations. However, in healthy individuals, measuring both AST and ALT may be redundant, leading to increased healthcare costs for the patient and the system, as well as unnecessary reagent consumption in cases where the simultaneous use of both markers is not justified. Therefore, the

aim of this study was to determine whether ALT alone is sufficiently sensitive and specific for detecting elevated AST levels in healthy individuals.

Methodology

Design and Study Population:

This was an analytical, retrospective, and cross-sectional study based on data extracted from the clinical records of medical consultations. The study was conducted from November 2021 to March 2023 at a polyclinic in the district of Villa El Salvador, Lima, Peru. Non-probability convenience sampling was employed, with the sample comprising the entire population that met the inclusion and exclusion criteria, totaling 846 patients.

The inclusion criteria were as follows: Patients aged 18 years or older who had been asymptomatic and healthy for the past six months, and who underwent examinations aimed at assessing their health status, with results that included concentrations of alanine aminotransferase and aspartate aminotransferase. Patients who were not healthy, those receiving treatment with drugs for chronic diseases (for example, diabetes or hypertension), as well as individuals who routinely used anti-inflammatory or analgesic medications for osteomyoarticular discomfort were excluded. In general, any patient who had taken any type of medication in the previous six months was excluded.

Variables and Measurements: The variables included sex, aspartate aminotransferase (AST), and alanine aminotransferase (ALT). The reference values for AST were 0 to 40 U/L, according to the parameters established by the laboratory that processed the samples. Clinical records and laboratory test results were collected and reviewed to ensure that the inclusion and exclusion criteria were properly applied. Data collection took place during medical consultations and preventive-promotional health campaigns held every third Wednesday from November 2021 to March 2023. The information was stored and organized using Microsoft Excel 2016, and subsequently analyzed using SPSS Statistics version 25.

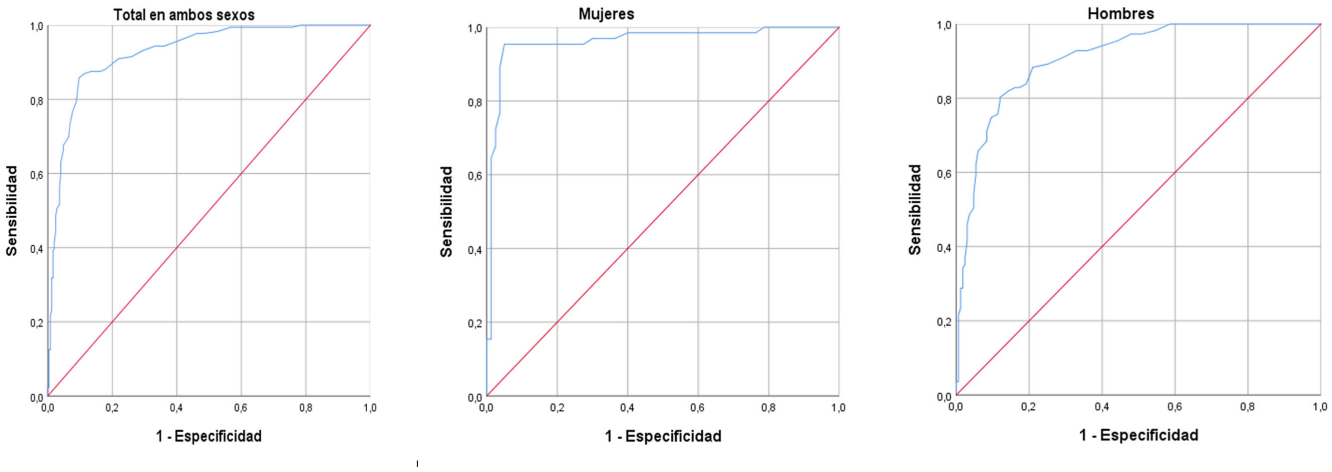
Statistical Analysis: The variables were dichotomized and arranged into 2 × 2 contingency tables. A Chi-square test was performed in the bivariate analysis to assess the association between variables. Phi coefficient and Cramér's V were used to evaluate the strength and direction of the association. A receiver operating characteristic (ROC) curve was generated to assess the sensitivity and specificity of the diagnostic test, considering ALT as a continuous variable in relation to AST. Additionally, a Chi-square good-

ness-of-fit test was used to determine normality; a p-value of 0.000 was obtained, which, being less than 0.05, indicated that the data did not follow a normal distribution. Finally, Spearman's correlation test was applied to evaluate the quantitative correlation, as the Kolmogorov-Smirnov test had confirmed non-normal distribution. A significance level of alpha = 0.05 was used as the decision threshold for statistical significance.

Ethical Considerations: The ethics committee of the polyclinic approved the study. All data were completely anonymous and consisted solely of numerical information; therefore, informed consent was not required. Only the principal investigator had access to the data.

Results: The area under the receiver operating characteristic (ROC) curve was 0.927 when considering the total population of both sexes, 0.961 in females, and 0.910 in males (Figure 1).

Figure 1. Receiver Operating Characteristic (ROC) Curve.



*Own Elaboration.

A statistically significant association was found for all variables. There was a high number of positive cases in both men and women. Likewise, the ROC curve values suggested that the optimal ALT cutoff point in women was 42.50 U/L, with a sensitivity of 84% and specificity of 85%; in men, 40.50 U/L with a sensitivity of 95% and specificity of 77%; and for the total population, 39.50 U/L with a sensitivity of 92% and specificity of 77% (Table 1).

Table 1. Characteristics of the ROC Curve, Sensitivity, and Specificity for Predicting AST Levels Based on ALT Levels in Adults

	Total	Female	Male
Positives	352	130	222
Negatives	494	160	334
Área	0.927	0.961	0.910
P	0.000	0.000	0.000
Lower limit	0.902	0.926	0.876
Higher limit	0.952	0.966	0.943
(+)if it is greater than or equal to	39.50	42.50	40.50
Sensibility	0.92	0.84	0.95
Specificity	0.77	0.85	0.77

*Own Elaboration.

A statistically significant association between ALT and AST was found, as well as a strong and positive relationship according to the Chi-square and Cramér's V tests. The Spearman correlation between the variables was high: 0.96 for the total sample, 0.83 in women, and 0.89 in men. Furthermore, men with elevated ALT levels were 82.81 times more likely to have elevated AST levels compared to men with normal ALT. Women with elevated ALT levels were 32.53 times more likely to have elevated AST than those with normal ALT. When considering both groups combined, regardless of sex, patients with elevated ALT levels were 42.84 times more likely to have elevated AST levels compared to those with normal ALT (Table 2).

Table 2. Measures of Association, Correlation, and Relative Risk Between ALT and AST in Healthy Adults

TGP-TGO	TOTAL	FEMALE	MALE
P	0.001	0.000	0.000
V de Cramer	0.698	0.688	7.52
OR	42.84	32.53	82.81
IC:95%	24.69-74.31	17.96-58.90	27.24-251.72
Rho	0.966	0.839	0.899

p-value < 0.05; OR: Odds Ratio; CI: Confidence Interval; Rho: Spearman Correlation

*Own Elaboration.

Discussion

The receiver operating characteristic (ROC) curve test, as well as the cross-tabulation tests performed using SPSS Statistics 25, showed that the measurement of ALT is highly sensitive and specific for diagnosing AST elevations in healthy adults. Other evidence supporting this relationship includes the high degrees of association and correlation observed in both men and women. The link between both enzymes has been recognized for decades from a pathological perspective, when in 1957, the use of the AST/ALT ratio was proposed as a marker of oxidative stress and systemic inflammation related to hepatitis B (17), a practice that was later extended to other acute and chronic pathological processes such as generalized infections, heart diseases, and vascular diseases (18), as well as directly associated with interleukins like IL-4, IL-6, and TNF-α, as mentioned in a study conducted in China in 2021 (19). On the other hand, a study on the relationship between transaminases and metabolic syndrome in adolescents found that these enzymes are significantly correlated and predict the development of obesity in adults (20). In a study on the AST/ALT ratio in patients with liver fibrosis, a high correlation was observed under these circumstances (21). Another study found that elevated levels of both enzymes strongly suggest the presence of liver failure, although their absence does not exclude it (22). However, the studies mentioned referred to specific diseases, while the present study demonstrates that the relationship between both aminotransferases is also strong in healthy individuals.

Furthermore, it was found through the Odds Ratio test that patients with high AST levels had a very high risk of elevated ALT in both sexes. This may be based on the fact that both aminotransferases are biologically close: ALT is primarily located in the cytosol of hepatocytes (23), and in smaller quantities in the heart, kidneys, muscles, bones, pancreas, etc. (24). In turn, AST is found not only in the cytosol but also in the mitochondria (25), and unlike ALT, it is distributed in similar proportions in the myocardium, liver tissue, skeletal muscle, lungs, erythrocytes, and other tissues (26). Both enzymes are released in greater amounts in the presence of acute or chronic inflammation (27). It was previously considered that a predominance of high ALT levels would inevitably indicate liver damage (28), and that a predominance of AST would be evidence of heart (myocardial infarction) or lung (lung cancer) damage (29). However, due to the knowledge that both enzymes are present in most tissues of the body, they are no longer considered sensitive

or specific markers for diseases (30). Therefore, the aforementioned studies mostly suggest using both markers as adjuncts or for follow-up.

Considering the results found in this study conducted in a healthy adult population, with high levels of association and correlation between both variables, and having found that the measurement of ALT levels is highly sensitive and specific for predicting AST alterations, in both healthy men and women undergoing health assessments, we can conclude that performing both tests simultaneously represents an unnecessary expense. It is recommended to perform the ALT test alone, as it is an enzyme that, in addition to allowing the evaluation of inflammatory processes in different organs, enables the assessment of liver status, which is the primary goal of the examination requested by patients, as it is included in the liver function panel.

The limitations of the study were related to the sample size, as well as the intentional convenience sampling method. Additionally, there is a possibility that some patients may have been developing diseases while remaining in an asymptomatic phase. Furthermore, patients may have unintentionally or intentionally failed to report having any acute or chronic illnesses, as well as engaging in harmful habits, which could have affected the results of this research.

In conclusion, the measurement of AST levels is highly sensitive and specific for ruling out glutamic oxaloacetic hypertransaminasemia in healthy adults evaluated at a polyclinic in Villa El Salvador, Peru. It is recommended that the findings of this study be extrapolated to larger populations. Moreover, it is considered appropriate for laboratories and primary and specialized care physicians to reconsider requesting both tests for healthy patients undergoing routine preventive health evaluations, in order to save economic resources and supplies. These resources could then be redirected toward the monitoring of diseases that genuinely require the use of both aminotransferases.

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Conflict of Interest: None.

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