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Original article

Performance of the AST/ALT Ratio as a Diagnostic Marker for Cholelithiasis: Insights from a Retrospective Study in Peruvian Patients with Biliary Colic

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Abstract

Objective: This study evaluated the association and diagnostic performance of the aspartate aminotransferase/alanine aminotransferase (AST/ALT) ratio in the detection of cholelithiasis in patients presenting with biliary colic. **Methods:** A cross-sectional retrospective study was conducted through the analysis of medical records of patients treated for biliary colic in the emergency department of a regional hospital in Peru. Confirmatory diagnosis of cholelithiasis was established based on clinical evaluation and abdominal ultrasonographic findings. Serum AST and ALT activity levels were obtained to calculate the AST/ALT ratio. Diagnostic performance was assessed using receiver operating characteristic (ROC) curve analysis. **Results:** A total of 191 medical records were reviewed, corresponding to 94 patients with cholelithiasis and 97 without. The mean age was 49.6 ± 15.1 years, and 72% of the cohort were women. Elevated ALT and AST levels were observed in 34% and 31.9% of patients, respectively. The area under the curve (AUC) for the AST/ALT ratio was 0.52, indicating minimal diagnostic value, while the AUCs for AST and ALT were 0.67 and 0.65, respectively. In the model adjusted for age and sex, the association between the AST/ALT ratio and cholelithiasis showed a prevalence ratio of 1.16 (95% confidence interval [CI]: 0.56–2.41). **Conclusion:** The AST/ALT ratio demonstrated limited efficacy as a diagnostic marker for cholelithiasis in patients with biliary colic. Although individual AST and ALT levels showed moderate diagnostic potential, the AST/ALT ratio did not significantly enhance the identification of cholelithiasis within this clinical context.

Keywords

Aspartate aminotransferase, alanine aminotransferase, AST/ALT ratio, cholelithiasis, biliary colic.

INTRODUCTION

Cholelithiasis, commonly known as gallstone disease, is a prevalent medical condition affecting between 5% and 20% of the general population[1]. Epidemiological evidence indicates a higher incidence in women than in men, as well as a greater burden in South American populations[2]. Cholelithiasis is a leading cause of biliary colic, characterized by severe abdominal pain resulting from obstruction of the biliary duct by gallstones[3]. In most cases, cholelithiasis is benign and is not associated with significant morbidity or mortality. However, in prolonged or severe cases, or in predisposed individuals, it may increase the risk of fibrosis and cirrhosis, hepatocellular carcinoma, or cholangiocarcinoma[4]. This condition not only represents a burden for healthcare systems but also significantly affects patients' quality of life[5].

The pathophysiology of cholelithiasis involves complex interactions among genetic predisposition, metabolic factors, and environmental influences. These interactions

lead to bile supersaturation with cholesterol or bilirubin and subsequent gallstone formation[6]. Despite advances in understanding the mechanisms underlying gallstone formation, early and accurate diagnosis of cholelithiasis remains a challenge in clinical practice[7], particularly in settings with limited imaging resources, the need for invasive diagnostic methods, or in cases involving "silent stones"[8], Mirizzi syndrome[9], and other atypical presentations.

The aspartate aminotransferase (AST) to alanine aminotransferase (ALT) ratio, known as the De Ritis ratio, is a key indicator of liver function and has traditionally been used to evaluate various hepatic disorders[10]. The AST/ALT ratio (De Ritis ratio) is useful for guiding the etiological assessment of hepatic dysfunction, as in alcoholic liver disease the ratio is typically >2. This pattern reflects mitochondrial injury and increased AST release, whereas in acute viral hepatitis and nonalcoholic fatty liver disease ALT elevation predominates and AST/ALT values are typically <1. However, in the latter condition, the ratio may increase as fibrosis progresses[11]. Recent studies have also associated this ratio with extrahepatic conditions such as insulin resistance[12], COVID-19[13], and increased risk of cardiovascular and all-cause mortality[14].

Some studies suggest that the AST/ALT ratio may also have diagnostic potential in biliary disorders[15,16]. Previous research has documented an association between liver enzyme abnormalities and biliary obstruction. However, the reported cutoff values vary widely[17,18], and choledocholithiasis has been reported to present with mild to moderate elevations of aminotransferases, generally up to 10 times the upper limit of normal, whereas higher levels are uncommon[19,20]. According to the American Society for Gastrointestinal Endoscopy (ASGE) guidelines, abnormalities in liver function tests together with age greater than 55 years constitute moderate predictors of choledocholithiasis, rather than uncomplicated cholelithiasis, as these criteria were designed to estimate common bile duct obstruction. Furthermore, subsequent updates excluded biliary pancreatitis as an independent predictor due to its negative association with choledocholithiasis. Therefore, these criteria should not be extrapolated to the diagnosis of isolated cholelithiasis[21].

Monitoring individuals at risk of cholelithiasis, in its various forms (intrahepatic or extrahepatic), should be ensured through multiple diagnostic methods. These include enzymatic markers such as alkaline phosphatase, γ-glutamyl transferase, and, in some cases, transaminases, to support prediction and diagnosis[22]. Assessment of transaminases provides valuable clinical information, and the De Ritis ratio may help differentiate cholelithiasis from other conditions, such as infectious or inflammatory processes; however, its routine use in clinical laboratories has not been widely reported[11,23].

In Peru, the prevalence of cholelithiasis is approximately 10%[24] and may reach up to 14% in asymptomatic cases[25]. Nevertheless, few publications have focused on specific risk groups, such as pregnant women[26] and populations living in high-altitude cities[27]. Peruvian clinical guidelines do not include these markers for early diagnosis[25], and the application of the AST/ALT ratio in the context of cholelithiasis remains insufficiently explored. This situation underscores the need to improve current understanding of the diagnostic potential of the AST/ALT ratio in biliary disorders.

METHODS

Ethical considerations

This study was approved by the Evaluation Committee of Universidad Alas Peruanas (Resolution No. 347-2019-FCS-EPTM-UAP). Authorization was also obtained from the General Management of Hospital II de Huamanga. As this study used retrospective patient data, informed consent was not required. However, all data were used exclusively for research purposes. Strict patient anonymity was maintained, and no personal identifiers were accessed.

Study design and population

This cross-sectional diagnostic test study, conducted in 2019 in the emergency department of Hospital Regional II de Huamanga (Ayacucho, Peru), evaluated the diagnostic performance and operating characteristics of the AST/ALT ratio for identifying cholelithiasis in patients with a clinical diagnosis of biliary colic.

The study population included patients diagnosed with biliary colic based on clinical presentation, primarily characterized by episodes of severe abdominal pain assessed using the visual analog scale. Patients were subsequently classified into two groups: those with confirmed cholelithiasis and those without cholelithiasis. The diagnosis of cholelithiasis[8] was established by abdominal ultrasound, considered the reference standard for gallstone detection. From a population of patients with a clinical diagnosis of biliary colic (presence of severe right upper quadrant pain, nausea, vomiting, fever, and chills reported within the previous 12 hours), two groups were defined: patients with ultrasonographic evidence of cholelithiasis and patients without gallstone findings on ultrasound. The latter constituted the comparison group for evaluating the diagnostic performance of the AST/ALT ratio.

Materials and procedures

Primary materials included medical records and laboratory results. Data collection was conducted systematically using a standardized form based on the review of medical records and routine biochemical test results. Serum enzymatic activity of AST and ALT was measured in samples obtained as part of routine clinical care using automated biochemical analyzers (Roche Diagnostics, Cobas c311, United States). Results were reported in international units per liter (IU/L). The AST/ALT ratio was calculated by dividing the AST value by the ALT value for each patient, with normal values defined as <40 U/L for AST and <45 U/L for ALT. No normal reference value has been established for the AST/ALT ratio in identifying cholelithiasis; however, previous studies[10,11] have defined values <1.0 as normal in individuals without liver disease.

Patients aged ≥18 years with biliary colic who underwent abdominal ultrasound were included. Two patients with hepatitis A infection and one patient with a history of cirrhosis were excluded. Data collection was performed by three individuals previously trained in the data collection process. All information was anonymized and recorded in a secure database for analysis.

Data analysis

Descriptive statistics were used to summarize demographic and clinical characteristics. The primary analysis employed receiver operating characteristic (ROC) curves to evaluate the diagnostic performance of the AST/ALT ratio for detecting cholelithiasis. The area under the curve (AUC) with a 95% confidence interval (CI) was calculated to determine discriminative ability. Additionally, the association between the AST/ALT ratio and the presence of cholelithiasis was analyzed using a generalized linear model with log link and Poisson distribution. The prevalence ratio (PR) was estimated with adjustment for age and sex, and statistical significance was defined as $p < 0.05$. The analysis was performed using Stata version 18 (StataCorp LLC, TX, United States).

RESULTS

A total of 191 medical records were evaluated, and patients were divided into two groups: 94 with cholelithiasis and 97 without cholelithiasis. The median age was 47 years, and women predominated (72.3%). In the biochemical analysis, 42.6% of patients in the cholelithiasis group presented elevated ALT activity and 41.5% elevated AST activity, according to the established reference values. Bivariate analysis showed significant differences in transaminase levels (AST and ALT) among patients with cholelithiasis, particularly for AST ($p < 0.001$). However, no significant difference was observed in the De Ritis ratio (**Table 1**).

Receiver operating characteristic (ROC) analysis evaluated the diagnostic performance of the AST/ALT ratio, as well as AST and ALT individually. The area under the curve (AUC) for the AST/ALT ratio was 0.52, indicating minimal discriminative ability. In contrast, the AUC values for AST and ALT were 0.67 and 0.65, respectively, indicating moderate diagnostic potential (**Figure 1**).

Table 1. Descriptive characteristics of the evaluated records (n = 191)

Characteristic	Cholelithiasis, n (%)		Value-*p*
	No (n = 97)	Yes (n = 94)	
Age (years)	47 (37-59)[a]	53 (39-62)[a]	0.082[c]
Sex			
- Male	25 (25.8)	28 (29.8)	0.536[b]
- Female	72 (74.2)	66 (70.2)	<0.001[c]
AST Activity (U/L)	30 (24-38)[a]	39 (29-48)[a]	0.002[c]
ALT Activity (U/L)	31 (25-42)[a]	38.5 (33-55)[a]	0.002[b]
Elevated AST			
- No	76 (78.4)	54 (57.4)	0.032[b]
- Yes	21 (21.6)	40 (42.6)	
Elevated ALT			
- No	71 (73.2)	55 (58.5)	0.592[c]
- Yes	26 (26.8)	39 (41.5)	
AST/ALT ratio	0.90 (0.77-1.11)[a]	0.87 (0.79-1.15)[a]	

[a]Median and interquartile range. [b]Pearson's chi-square test. [c]Mann–Whitney U test. Table prepared by the authors.

The association between the AST/ALT ratio and cholelithiasis, assessed using a generalized linear model, showed a crude prevalence ratio (PR) of 1.19 (95% confidence interval [CI]: 0.57–2.47). After adjustment for age and sex, the PR was 1.16 (95% CI: 0.56–2.41) (**Table 2**).

DISCUSSION

The present study evaluated the diagnostic performance of the De Ritis ratio for detecting cholelithiasis in patients presenting with biliary colic. The findings indicate that the AST/ALT ratio does not significantly differentiate between individuals with and without cholelithiasis; therefore, its applicability as a biomarker in this specific clinical context appears limited, with a limited discriminative capacity of the AST/ALT ratio observed for distinguishing cholelithiasis

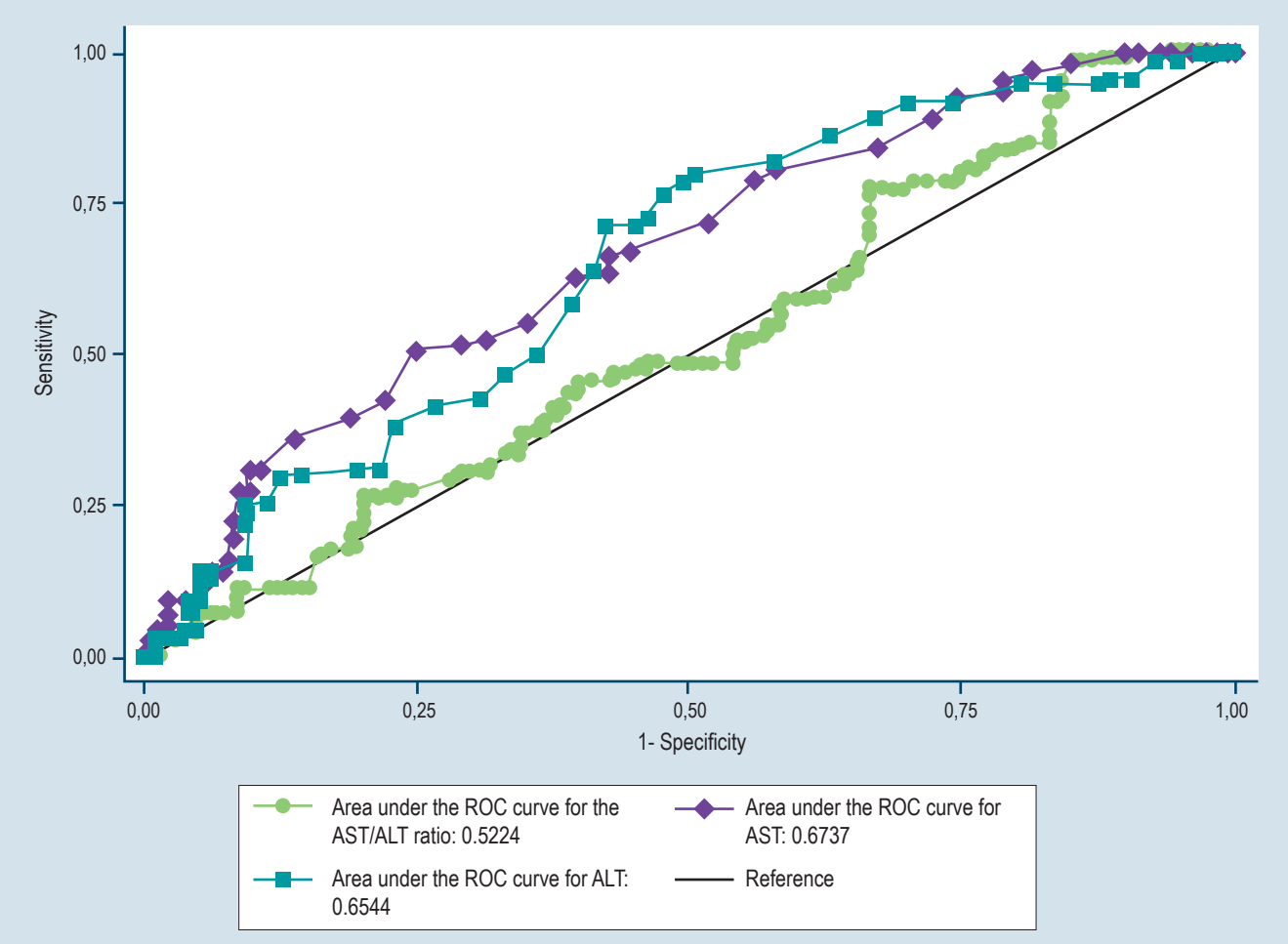

Figure 1. Diagnostic performance of the AST/ALT ratio and the independent enzymatic activity of AST and ALT. Image property of the authors.

Table 2. Association between the AST/ALT ratio and cholelithiasis in multivariable analysis

Independent variables	Crude model[a]			Adjusted model[a]		
	PR	95% CI	*p*-value	PR[b]	95% CI	*p*-value
AST activity (U/L)	1.01	1.00-1.02	0.017	1.01	1.01-1.02	0.024
ALT activity (U/L)	1.01	1.00-1.01	0.084	1.01	1.00-1.01	0.109
AST/ALT ratio	1.19	0.57-2.47	0.644	1.16	0.56-2.41	0.689

[a]GLM (Poisson family with log link). [b]Adjusted for age and sex. ALT: alanine aminotransferase; AST: aspartate aminotransferase; CI: confidence interval; PR: prevalence ratio. Table prepared by the authors.

from other causes of biliary colic. With an AUC of 0.52, the index exhibited only minimal diagnostic utility, a finding that contrasts with its well-established value in other hepatic and extrahepatic conditions[3]. A plausible explanation for these results may lie in the pathophysiological differences between cholelithiasis and other liver diseases in which the AST/ALT ratio has demonstrated diagnostic relevance[11]. Studies of hepatic conditions such as viral hepatitis and alcoholic liver disease have shown the usefulness of this index in those contexts, which suggests that its diagnostic value may

be condition-specific[28]. Unlike these disorders, cholelithiasis primarily affects the biliary tract rather than the hepatic parenchyma, which may explain the absence of significant alterations in the AST/ALT ratio in this setting[29].

When evaluated individually, transaminase activity (AST and ALT) demonstrated moderate diagnostic performance (AUC = 0.67 and 0.65, respectively). This suggests that isolated elevations of these enzymes may reflect pathophysiological processes associated with the disease, although their utility as standalone diagnostic tests is limited. Enzymatic elevations in cholelithiasis are typically transient and associated with episodic biliary obstruction, which may not be adequately captured by the AST/ALT ratio alone[30]. Another possible explanation is that enzymatic activity in cholelithiasis may be influenced by factors such as intermittent obstruction or coexisting hepatic conditions, which may obscure the relationship between the AST/ALT ratio and the presence of gallstones[18].

These findings are consistent with existing literature suggesting the need for more specific biomarkers for the diagnosis of cholelithiasis and underscore the importance of contextual interpretation of hepatic enzyme abnormalities[19]. Previous studies have highlighted the limitations of traditional hepatic biomarkers in differentiating biliary pathologies. For instance, Contreras-Omaña et al. proposed that elevated AST and ALT levels represent a "cholestatic" pattern of bile duct obstruction and that this differentiation may be achieved through indices incorporating alkaline phosphatase and ALT levels, in which values below 2 suggest cholestasis[31]. This observation is relevant because it indicates that cholelithiasis may be associated with mild to moderate hepatic injury. Furthermore, it is essential to recognize that cholelithiasis is inherently a chronic condition[32]. However, the present study did not include data regarding the extent of gallstone disease, which would have enabled a more comprehensive analysis.

It is important to distinguish between gallbladder cholelithiasis and choledocholithiasis. Some clinical guidelines have proposed abnormalities in liver function tests as predictors of common bile duct obstruction. However, these criteria were developed to estimate the risk of choledocholithiasis and not to diagnose uncomplicated cholelithiasis[21,25]. Extrapolation of these parameters to isolated gallbladder disease may lead to misinterpretation. This reinforces the need to contextualize the use of hepatic biomarkers according to the specific clinical scenario.

Despite the novelty of this finding, the results may be limited by the retrospective design and reliance on medical records, which may introduce selection bias or incomplete data capture. Additionally, ultrasonography is not the definitive reference standard for cholelithiasis, and magnetic resonance cholangiography would have provided a more robust diagnostic reference. However, the regional hospital lacks access to this technology. Furthermore, the study was conducted in a single regional hospital in Peru, which may limit generalizability to other populations or healthcare settings. Notably, this is the first study to critically evaluate the diagnostic utility of the AST/ALT ratio specifically in the context of cholelithiasis within a Peruvian population.

This study highlights the importance of a contextualized evaluation of diagnostic tools and suggests that reliance solely on the AST/ALT ratio for diagnosing cholelithiasis is not advisable without supporting evidence. Although the AST/ALT ratio has demonstrated value in the assessment of certain hepatic conditions, the present findings indicate that its diagnostic utility for cholelithiasis is limited.

CONCLUSION

This study provides the first comprehensive evaluation of the AST/ALT ratio as a diagnostic tool for cholelithiasis in a Peruvian hospital setting. The findings suggest that reliance solely on the AST/ALT ratio may be insufficient for accurately diagnosing cholelithiasis. This underscores the need for more reliable biomarkers in clinical practice.

Further research is required to identify alternative biomarkers or combinations of markers that may improve the diagnostic accuracy of cholelithiasis. Future studies should involve larger multicenter cohorts to validate these findings and to assess the integration of additional clinical parameters or novel biochemical markers. Longitudinal studies may also provide insight into the temporal dynamics of hepatic enzymatic alterations as cholelithiasis progresses. Such evidence may facilitate identification of early indicators of disease development.

The identification of alternative biomarkers or composite diagnostic criteria tailored to the pathophysiological characteristics of cholelithiasis may improve diagnostic accuracy and optimize the clinical management of patients with this prevalent condition.

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Institutional review board statement

This study was approved by the Evaluation Committee of Universidad Alas Peruanas (Official Letter No. 347-2019-FCS-

EPTM-UAP). Authorization was also obtained from the General Management of Hospital II de Huamanga.

Informed consent statement

As this retrospective study used human data, informed consent was not required.

Data availability statement

Data supporting the findings of this study are available from the corresponding author upon reasonable request.

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Conflicts of interest

The authors declare no conflicts of interest.

Authors' contributions

TL, LRT, JL, GBQ, and JRR contributed as follows. TL: conceptualization, methodology, data curation, formal analysis, investigation, writing – original draft. LRT: data curation, investigation, formal analysis, writing – review and editing. JL: data curation, formal analysis, visualization, writing – review and editing. GBQ: validation, writing – review and editing, project administration. JRR: conceptualization, methodology, formal analysis, supervision, writing – original draft, writing – review and editing, project administration. All authors read and approved the final version of the manuscript.

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