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Original Research Article

Analysis of the De Ritis ratio in different diseases: an observation in a tertiary care hospital

Tanisha Ray[1], Asitava Roy[2], Satadal Das[3]*

[1]Amity Institute of Biotechnology, Amity University, Kolkata, West Bengal, India
[2]Department of Biochemistry, Peerless Hospital and B. K. Roy Research Centre, Kolkata, West Bengal, India
[3]Department of Microbiology, Peerless Hospital and B. K. Roy Research Centre, Kolkata, West Bengal, India

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***Correspondence:**
Dr. Satadal Das,
E-mail: drsatdas@hotmail.com

ABSTRACT

Background: One useful biomarker for hepatic and extra-hepatic disorders is the De Ritis ratio of serum aspartate aminotransferase/ alanine aminotransferase (AST/ALT). There is growing evidence that it affects the prognosis of diseases related to the heart, metabolism, nervous system, and kidneys. In a tertiary care context, this study sought to assess its variation among age groups and systemic disorders.
Methods: Over the course of two months in 2025, a cross-sectional study was carried out at Peerless Hospital in Kolkata. There were 25 controls and 344 cases. Clinical diagnosis was used to categorize participants into groups related to gastrointestinal, cardiovascular, metabolic, neurological, kidney, and gynaecological conditions. The De Ritis ratio was computed and AST and ALT levels were tested. Data were stratified by age and analysed using Pearson correlation.
Results: The De Ritis ratio was elevated in all disease groups compared to controls. Cardiovascular patients aged between 31-60 years had the highest ratios. Metabolic, gastrointestinal, and neurological disorders showed progressive increases with age. Kidney disease (KD) patients had the highest ratios in elderly groups. Strong positive correlations were observed between gastrointestinal and neurological ($r=0.95$, $p<0.00001$), and between metabolic and neurological groups ($r=0.75$, $p=0.0047$). A strong negative correlation existed between cardiovascular and metabolic groups ($r=-0.76$, $p=0.0044$).
Conclusions: The De Ritis ratio's wide range of applications beyond hepatology is supported by the notable variance it exhibits with age and disease type. Our study demonstrates that it could be a helpful prognostic marker for a variety of systemic diseases.

Keywords: De Ritis ratio, Liver function test, Systemic diseases, Prognostic marker, Tertiary care hospital, Cross-sectional study

INTRODUCTION

The De Ritis ratio, the ratio of AST to ALT, was introduced by Fernando De Ritis in 1957.[1] This ratio is a very intricate biochemical metric providing a wealth of metabolic data.[2] It remains a simple yet powerful diagnostic and prognostic tool in hepatology. AST and ALT are enzymes released into the bloodstream during liver cell damage. ALT is found mainly in the cytoplasm of hepatocytes, while AST exists in both cytoplasm and mitochondria of hepatocytes.[1] The normal serum levels of AST and ALT are similar despite AST's greater abundance in liver tissue because of differences in clearance rates (AST: 18 h, ALT: 36 h).[1] AST is found in multiple tissues including the liver, cardiac muscle, skeletal muscle, kidneys, brain and red blood cells, whereas ALT is predominantly localized in the cytoplasm of hepatocytes, making it more specific to liver injury.[4] Important metabolic connections between the metabolism of amino acids and carbohydrates are represented by the ALT and AST catalysed processes.[3] In order to produce oxaloacetic acid and pyruvic acid respectively, the enzymes AST and ALT catalyse the transfer of alpha-

amino groups from aspartate and alanine to the alpha-keto group of ketoglutaric acid. Both enzymes need pyridoxal-5'-phosphate (vitamin B6) to perform this reaction, however ALT activity is more affected by pyridoxal-5'-phosphate deficit than AST activity is.[4] Although the exact mechanisms underpinning the cells' release of ALT remain unknown, they could include cytoplasmic budding or blebbing or cellular leakage. Cellular death, direct tissue injury, plasma membrane blebs breaking out from the cell membranes releasing cytoplasmic material, enhanced AST gene expression and macro enzymes are the five main mechanisms that account for the elevation of AST in blood.[3] The normal serum AST levels for males and females range from 17-59 U/l and 14-36 U/l respectively. The normal serum ALT levels for males and females range from 21-72 U/l and 9-52 U/l respectively. In healthy individuals, AST and ALT levels are about equal, giving a ratio around 1.0.

Changes in the De Ritis ratio can provide insights not only into liver damage but also into extra-hepatic disorders. A ratio less than 1 is typically seen in acute viral hepatitis and non-alcoholic fatty liver disease (NAFLD), reflecting a predominant elevation in ALT. Conversely, a ratio greater than 2 is often associated with alcoholic liver disease, advanced fibrosis, or conditions involving muscle injury, where AST levels may be disproportionately elevated.[4,5] Since AST is abundant in muscle, elevations without parallel ALT rise suggest muscle injury rather than liver disease. Exercise induced AST elevations may mislead clinicians unless CK levels are considered.[1] For instance, vigorous exercise like lifting weights can raise AST to 100-1000 U/l and ALT to 50-200 U/l.[6] In recent years, the De Ritis ratio has gained renewed interest due to its prognostic implications. Studies have demonstrated that this ratio can help predict disease severity, monitor treatment outcomes and even correlate with histopathological findings. It has also been linked with mortality risk in critically ill patients, particularly those with sepsis, chronic KD (CKD) and cardiovascular complications.[7,8] Patients with myocardial infarction, atrial fibrillation and heart failure have been observed to have cardio-hepatic interactions.[9] Numerous studies have shown that liver dysfunction is frequently present in people with cardiovascular disease (CVD). Only a small number of those studies were carried out on people with obvious coronary artery disease or acute myocardial infarction, though the majority of them deal with patients who have chronic heart failure. Transaminases such as AST and ALT may serve as predictive indicators for a patient's fate following an acute cardiac event, according to new research.[10]

A 2020 research study showed that total occlusion during acute myocardial infarction is strongly predicted by AST/ALT $\geq$2.[11] A small number of studies have demonstrated that a high AST/ALT ratio is independently associated with the elevated risk of death and complications in individuals with cerebrovascular events.[12] One of the main causes of death across the world is stroke. Prior research has demonstrated a correlation between AST and ALT levels and functional outcomes following an acute ischemic stroke. Following an ischemic stroke, excessive glutamate production by neurons raises intracellular calcium in neurons. As a result, neural cell death is triggered by high intracellular calcium levels. Consequently, elevated blood glutamate causes AST and ALT levels to rise, which causes glutamate to be eliminated from the peripheral circulation.[13]

The De Ritis ratio has also been linked to CKD. In the twenty-first century, the rising incidence of obesity, diabetes mellitus and hypertension, together with population aging are the main causes of CKD, which is becoming a significant public health concern. Whatever the underlying cause, CKD is characterized by slow progression that leads to end-stage renal disease, permanent nephron loss and early death. Increased AST/ALT ratio has been linked to oxidative stress, inflammation and insulin resistance, all of which are common in patients with CKD. A study conducted among American adult CKD patients showed that there is a positive correlation between the De Ritis ratio and the risk of all causes and CVD mortality in these patients.[14] Studies conducted since the 1970s have demonstrated that CKD patients receiving haemodialysis have lower serum levels of AST and ALT. The withdrawal of aminotransferases during haemodialysis session, high lactate serum levels that would quickly consume nicotinamide adenine dinucleotide phosphate during biochemical dosages, the presence of uremic factors that would inhibit the activity of these enzymes, and, lastly pyridoxine deficiency, a cofactor for the synthesis of the aminotransferases, were all thought to be potential causes of this reduction.[15]

The liver plays a major role in the onset of type 2 diabetes mellitus (T2DM) and insulin resistance. T2DM and NAFLD are correlated in both directions. In the meantime, non-alcoholic steatohepatitis (NASH), an inflammatory consequence of NAFLD, develops in many T2DM patients.[16] In few studies it has also been shown that insulin resistance and metabolic syndrome are linked to the ratio of AST to ALT. It has been suggested that AST/ALT ratio serves as a surrogate marker for insulin resistance and hyperinsulinemia. According to recent research, the development of metabolic syndrome in the future is inversely correlated with an elevated AST/ALT ratio. Therefore, when the AST/ALT ratio is less than 0.93, it is plausible to believe that AST/ALT is inversely linked with the development of T2DM.[17] Several epidemiological studies have linked CVD and metabolic syndrome to abnormal liver enzymes, even in the absence of liver damage or steatosis. For example, increased ALT levels have been linked to long-term metabolic problems in Framingham offspring heart study participants.[18]

In the context of a tertiary care hospital, where patients with a wide array of acute and chronic conditions are present, the evaluation of the De Ritis ratio can provide valuable diagnostic and prognostic information. The purpose of this study is to evaluate the trend of the

AST/ALT ratio in relation to different age groups and various systemic diseases seen at a tertiary healthcare facility.

METHODS

Study design and setting

This was a hospital based, cross-sectional study. It was conducted in the department of biochemistry at Peerless Hospital and B. K. Roy Research Centre, a tertiary care hospital located in Kolkata, West Bengal, India. The study was carried out over a period of 2 months from 20th May 2025 to 20th July 2025.

Study population

A total of 344 patients, admitted to the Peerless hospital with various clinical diagnoses were enrolled in the study. Out of these 344 patients, 184 patients were males and 160 patients were females. A separate group of 25 pre-operative individuals admitted for minor, non-systemic surgical conditions, served as the control group. Individuals in the control group had normal results for liver function tests (specifically the AST and ALT levels were within the biological reference range). The control group provided a baseline reference for AST/ALT values and the De Ritis ratio in a healthy population.

Inclusion and exclusion criteria

Patients included in our study had the following criteria: patients aged ≥18 years, patients were diagnosed with any one of these diseases such as gastrointestinal disorders/cardiovascular disorders/metabolic disorders/neurological disorders/kidney disorders/gynaecological disorders, serum AST and ALT levels outside the biological reference range and confirmed clinical diagnosis based on supporting investigations and physician assessment. Patients excluded from our study had the following criteria: patients <18 years of age and patients with incomplete biochemical records i.e. missing AST and ALT values.

Sample collection and analysis

Approximately 5 ml of venous blood sample was collected under aseptic conditions from each patient using a sterile needle in SST. SST is a serum separator tube designed to facilitate the separation of serum from blood sample. These tubes contain a clot activator to speed up clotting and a gel that forms a barrier between serum and blood cells during centrifugation. After blood samples were collected in those tubes, those samples were allowed to clot and then centrifuged at 4000 rpm for 15 minutes to separate the serum. Then routine liver function tests were performed using those serum samples with the help of VITROS 5600 integrated system which is an automated clinical chemistry analyser, following standard operating procedures with appropriate quality control.

Study parameters

Serum LFT details of each patient included the following parameters: Total bilirubin (expressed in mg/dl), direct bilirubin (expressed in mg/dl), indirect bilirubin (expressed in mg/dl), total protein (expressed in g/dl), albumin (expressed in g/dl), globulin (expressed in g/dl), SGPT (ALT) (expressed in U/l), SGOT (AST) (expressed in U/l), ALP (expressed in U/l), GGT (expressed in U/l). But only serum ALT and AST levels for each patient was taken into consideration. For our study, the clinical diagnosis and serum LFT details of each patient were collected from laboratory information systems. During this study demographic details of the patients like age and sex were also taken into consideration. The AST/ALT ratio was calculated for each patient from the AST and ALT values.

Classification by disease groups

Patients were categorized based on their clinical diagnosis into the following groups: Group 1: control group-25 individuals, group 2: gastrointestinal disease (GID)-70 individuals, group 3: CVD-56 individuals, group 4: metabolic disease (MD)-138 individuals, group 5: neurological disease (ND)-53 individuals, group 6: KD-17 individuals and group 7: gynaecological disease-10 individuals.

Statistical analysis

The primary outcome variable in this study was the De Ritis ratio (AST/ALT). Different groups of patient data were first entered into Microsoft Excel version 2021 for preliminary checks and further analysis. Then the patients from each disease group were categorized into the following subgroups based on their age: Age-group 1: 1-10 years, group 2: 11-20 years, group 3: 21-30 years, group 4: 31-40 years, group 5: 41-50 years, group 6: 51-60 years, group 7: 61-70 years, group 8: 71-80 years, group 9: 81-90 years and group 10: >90 years.

Using the calculator.net standard deviation calculator, the De Ritis ratio for each subgroup was calculated and expressed as mean±standard deviation (SD)±standard error of the mean (SEM). SEM was computed to assess the precision of the sample mean.

To find out the Pearson correlation coefficient (r) between the mean De Ritis ratios of different age groups across different systemic diseases, we used Pearson correlation coefficient calculator by social science statistics. Pearson's correlation was used to determine the strength and direction of linear association between age (continuous variable) and De Ritis ratio (continuous variable).

Using the same software, corresponding p value was also computed to assess the statistical significance of each correlation. A $p<0.05$ was considered statistically significant.

RESULTS

The present study analysed the De Ritis (AST/ALT) ratio across different systemic diseases in various age groups. A total of 369 participants (344 patients and 25 controls) were enrolled, distributed among the following disease categories: GID (n=70), CVD (n=56), MD (n=138), ND (n=53), KD (n=17), gynaecological disease (GD) (n=10) (Figure 1).

AST/ALT ratio by age group

In the control group the De Ritis ratio remained within the normal range (1.0-1.4) across age groups with minimal fluctuations. In contrast, disease groups showed marked age-dependent variations:

CVD patients exhibited significantly elevated De Ritis ratios, specifically in the 31-40, 41-50, 51-60 years age groups, reaching upto 3.65±2.28±0.93. In MD patients, the ratio was elevated across all age groups but peaked in elderly groups (e.g. 1.8±1.10±0.34 in 81-90 years age group). GID patients also demonstrated rising ratios with age, with the highest value being 3.6±2.92±1.46 in the 81-90 years group. ND patients showed progressive increases with age, notably in the 71-90 years bracket, with a peak of 3.6±2.34±1.17. In KD group the highest mean De Ritis ratio (3.08) was observed in the 61-70 years age group, suggesting an age-associated elevation in the ratio. The De Ritis ratio in the GD group showed no consistent age-related trend, probably due to heterogeneous nature of gynaecological conditions (Table 1).

Correlation between disease groups

GID vs CVD: A moderate negative correlation was observed (r=-0.4722, p=0.1211). GID vs ND: A strong positive correlation was found (r=0.9497, p=<0.00001), statistically significant at <0.01 level. GID vs MD: A fairly strong positive correlation was noted (r=0.8757, p=0.000041), statistically significant at <0.01 level. CVD vs ND: A moderate negative correlation was found (r=-0.5072, p=0.0923), which is marginally significant. CVD vs MD: A fairly strong negative correlation was observed (r=-0.7561, p=0.0044), statistically significant at <0.01 level. ND vs MD: A fairly strong positive correlation was observed (r=0.7522, p=0.0047), statistically significant at <0.01 level (Table 2).

Table 1: Mean De Ritis ratios in different age groups across various diseases.

Age group (in years)	Controls, (n=25)	GID, (n=70)	CVD, (n=56)	MD, (n=138)	ND, (n=53)	KD, (n=17)	GD, (n=10)
1-10	0	0	0	0	0	0	0
11-20	0	1.23±0.92± 0.53 (3)	1	1	0	0	0
21-30	1	0.47±0.26± 0.13 (4)	0	0.81±0.63± 0.21 (9)	1.02±0.80± 0.40 (4)	1	1.33±1.36± 0.78 (3)
31-40	1±0.42± 0.3 (2)	1.31±1.15 ±0.27 (17)	3.18±2.17± 0.97 (5)	1.3±1.16± 0.32 (13)	0.85±0.61± 0.19 (10)	0	1
41-50	1.16±0.40± 0.23 (3)	1.03±0.72± 0.22 (10)	3.65±2.28± 0.93 (6)	1.06±0.48± 0.11 (18)	1.4±1.83± 0.69 (7)	2.5±1.11± 0.64 (3)	0.66±0.40± 0.18 (5)
51-60	1.05±0.13± 0.05 (6)	2±1.05± 0.39 (7)	3.01±2.49± 0.71 (12)	1.26±0.91± 0.19 (23)	2.18±1.69± 0.75 (5)	2.22±1.59± 0.79 (4)	0
61-70	1.4±0.51± 0.23 (5)	1.48±0.99± 0.25 (15)	2.24±1.72± 0.46 (14)	1.55±1.21± 0.22 (30)	1.74±1.37± 0.36 (14)	3.08±0.92± 0.41 (5)	0
71-80	1.22±0.50± 0.22 (5)	2.24±2.68± 0.84 (10)	2.15±1.82± 0.52 (12)	1.47±1.20± 0.20 (33)	2.5±1.77± 0.59 (9)	1.77±1.17± 0.58 (4)	0
81-90	1.33±0.61± 0.35 (3)	3.6±2.92± 1.46 (4)	2.6±1.97± 0.80 (6)	1.8±1.10± 0.34 (10)	3.6±2.34± 1.17 (4)	0	1
>90	0	0	0	1	0	0	0

*Showing the AST/ALT ratios (Mean±SD±SEM) in different age groups across different systemic diseases.

Table 2: Correlation between disease groups.

Controls	GID	CVD	ND	MD
GID	0.3932 (0.206)			
CVD	-0.6466 (0.023)**	-0.4722 (0.1211)		
ND	0.53 (0.076)*	0.9497 (<0.00001)****	-0.5072 (0.0923)*	
MD	0.6891 (0.0131)***	0.8757 (0.000041)****	-0.7561 (0.0044)****	0.7522 (0.0047)****

*Showing Pearson's correlation matrix of ratios between different age groups in different systemic diseases. Values in parentheses are p values, indicating the statistical significance of each correlation. [*marginally significant, **significant at 0.05 level, ***significant at 0.01 level, ****significant at <0.01 level].

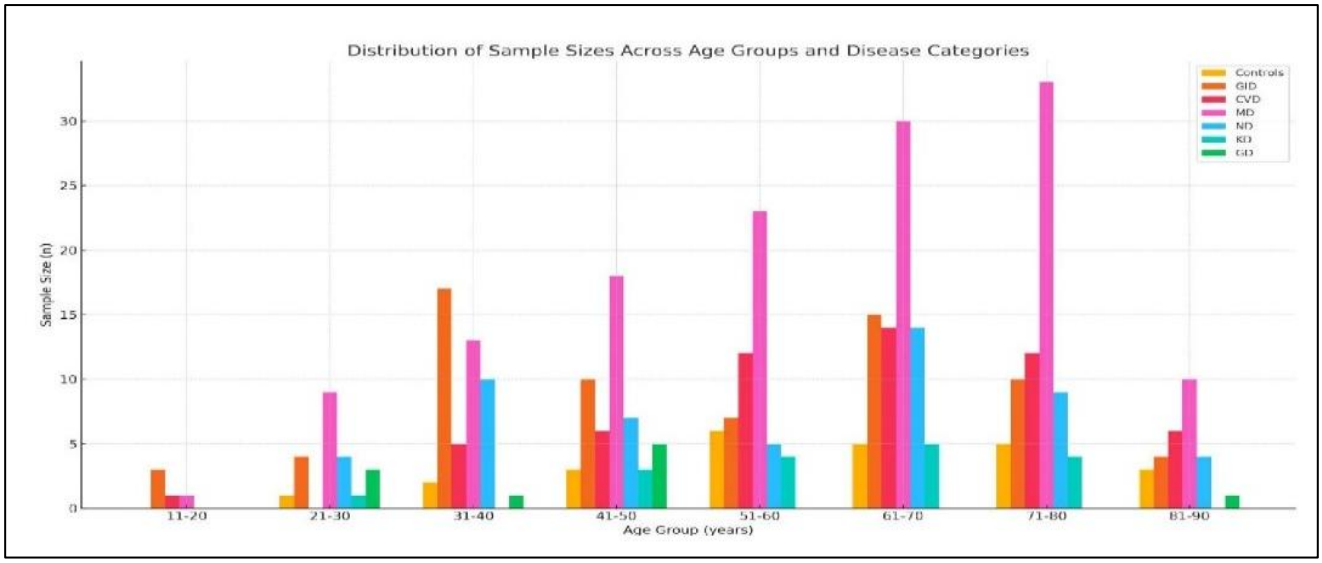

Figure 1: Distribution of sample sizes across different age groups and disease categories.

A visual comparison of the age distribution among the study groups is provided by each bar, which shows the number of individuals in that age group for each disease category.

DISCUSSION

The De Ritis ratio is a well-established biochemical marker, primarily used to differentiate types of liver diseases. In liver diseases, a high AST:ALT ratio is predictive of poor prognosis. Increased AST:ALT ratio in liver diseases indicates release of AST from mitochondria which is almost always associated with advanced liver damage and thus less chance of survival.[19] De Ritis ratio is a prognostic indicator in certain KDs like CKD and renal cell carcinoma.[20] This ratio is also an indicator of prognosis in some NDs like Alzheimer's disease and acute ischemic stroke.[21] De Ritis ratio is also an indicator of prognosis in some muscular diseases like polymyositis and dermatomyositis.[22] The AST/ALT ratio is even related to prognosis in CVDs and increased ratios are linked to increased risk of cardiovascular events and mortality.[3]

Age-related trends

This study reveals that the De Ritis ratio tends to increase with age in patients with cardiovascular, metabolic, gastrointestinal and neurological conditions. This ratio usually increases with age due to declining ALT levels by oxidative stress, increased AST levels due to sarcopenia and gradually degrading tissue health.[23] In CVD patients, ratios were significantly elevated in middle-aged adults aligning with the findings by Giannini et al who noted that cardiovascular stress can increase AST disproportionately due to its extra-hepatic sources.[4] The progressively increasing De Ritis ratio in KD patients may be attributed to uremic liver dysfunction, reduced hepatic clearance or extrahepatic sources of AST. The pattern supports previous findings that CKD can result in altered liver enzyme levels due to both metabolic and inflammatory stress.[24]

Inter-disease correlation

A strong correlation between GID and ND (r=0.9497) suggests shared systemic or inflammatory processes that progressively impact liver enzyme levels with aging. A strong positive correlation between MD and ND (r=0.7522) implies a potential trend of similar age-related increases in the De Ritis ratio. Conversely the strong negative correlation between CVD and MD (r=-0.7561) indicates an opposing trend of De Ritis ratio changes with age between CVD and MD. It suggests possible mitochondrial injury or muscle-related AST elevations in cardiac conditions. This is consistent with previous findings where elevated AST in CVD patients originates from cardiac muscle, not hepatocytes.[7] A moderate negative correlation between CVD and ND (r=-0.5072) indicates that with increasing age the De Ritis ratio in CVD tends to move inversely to that in ND. Due to the limited sample size of both KD and GD groups direct statistical correlation values were not calculated. But the high De Ritis ratio in elderly KD patients aligns more closely with the trends seen in CVD and ND groups.

Diagnostic significance

De Ritis ratios were consistently high in patients with CVD, frequently surpassing 3.0. Given that AST has a myocardial origin, it is possible that high De Ritis ratios in these situations more accurately represent cardiac muscle injury than hepatic pathology. Across all age categories, the De Ritis ratio in MDs remained high, which can be a reflection of the fatty liver alterations and persistent low-grade inflammation found in diseases like type 2 diabetes and obesity. In line with recent research highlighting its usefulness beyond liver dysfunction, this validates its role as a prognostic biomarker in metabolic disorders.[25]De

Ritis ratios were considerably higher in aged ND patients (up to 3.6), which may indicate systemic inflammation, catabolism or multi-organ stress instead of direct liver injury. Patients with GID had varying ratios; those aged 81 to 90 had values >3.5, indicating systemic comorbidities in chronic GI conditions or significant liver involvement.

Despite these fascinating findings, our study has several limitations. Because the study was cross-sectional, it was difficult to determine a causal link between high De Ritis ratios and the course or results of the disease over time. Sample sizes were comparatively limited for some disease categories, including gynaecological disease (n=10) and KD (n=17). For these categories, this hindered a thorough inter-group correlation analysis and decreased the statistical power. The results may not apply to other populations or healthcare settings with distinct clinical and demographic features because the study was limited to a single tertiary care hospital in Kolkata.

CONCLUSION

Beyond conventional hepatology, the current investigation supports the usefulness of the De Ritis ratio (AST/ALT) as a flexible, easily obtainable and clinically significant biomarker for assessing disease-related changes in liver enzymes. Our results show that the De Ritis ratio changes dramatically across a range of systemic diseases and not only reflects hepatic impairment but also corresponds with age. Although this study offers strong support for the De Ritis ratio's diagnostic utility, there are a few areas that need more research: longitudinal studies can help determine whether the De Ritis ratio acts as a prognostic marker for disease progression, complications or mortality; studies involving liver histopathology or imaging correlation would help us with the mechanistic understanding of enzyme alterations; larger, multicenter studies are required to validate these findings across a variety of populations and healthcare facilities. In conclusion we can say that despite its simplicity, the De Ritis ratio has a lot of unrealized potential in contemporary clinical diagnosis.

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