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ORIGINAL ARTICLE

The Prognostic Role of In-Hospital Mortality Predictors and De Ritis Ratio in Patients with Upper Gastrointestinal System Bleeding

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ABSTRACT

Objective: We aimed to evaluate the prognostic significance of the aspartate aminotransferase(AST) / alanine aminotransferase (ALT) named as (De Ritis) ratio in patients hospitalized in the intensive care unit with the diagnosis of upper gastrointestinal (GI) bleeding.

Method: We retrospectivelyanalyzed the clinical and laboratory data of 243 patients admitted with upper GI bleeding to the intensive care unit of our tertiary hospital between January 2018 and April 2022. The potential prognostic parameters between survivors and non-survivors groups and then between low De Ritis and High De Ritis groups were compared. The effect of the De Ritis ratio on in-hospital mortality was investigated by logistic regression analysis.

Results: Of the two hundred andforty-three patients hospitalized with upper GI bleeding, 65.8% were male. The mean age of the patients was 68.6±11.56. The cut-off value for low and high De Ritis groups was selected as 1.57,which value seperated second tertile and third tertile of the patient population.İn hospital mortality rate was 13.1%.

While albumin level was higher in the low De Ritis group, ALT, AST, and INR values were higher in the high De Ritis group. No statistically significant correlation was found between these two groups in terms of mortality. Moreover, De Ritis ratio did not show a significant difference between survivors and non-survivors (p=0.058).

Conclusion: It was concluded that the rate of De Ritis is not an independent predictive factor for mortality in patients with upper GI bleeding. But, more prospective and randomized studies are needed to evaluate clearly the prognostic value of the De Ritis ratio in upper GI bleeding patients.

Keywords: De Ritis ratio, aspartate aminotransaminase, alanineaminotransaminase, upper gastrointestinal bleeding, mortality

INTRODUCTION

Upper gastrointestinal (GI) system bleeding is a life-threatening condition that requires urgent diagnosis and treatment. Although its mortality has decreased over the years with the introduction of proton pump inhibitor group drugs and the developments in endoscopic treatments, the mortality rate can reach 10% today. (1, 2) For this reason, studies have been conducted on predictive parameters and risk scoring to predict mortality in patients with GI bleeding. Thus, by separating the high-risk patient group from the lower-risk patient group, it was aimed to identify patients who require close monitoring and more careful follow-up, optimize their treatments, and so to reduce mortality.

Advanced age, chronic liver disease, chronic kidney insufficiency, advanced malignancy, low hemoglobin level, and heart failure are among the parameters previously shown to predict GI bleeding mortality. (3-7) Today, the use of biomarkers to accelerate diagnostic processes and predict prognosis becomes widespread and clinical studies on new biomarkers increase day by day. These markers are expected to assist the clinician in predicting the patient's risk and prognosis. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are also widely used and easily accessible biomarkers. It is thought that the ALT value is mostly related to liver-related pathologies and its increased level reflects the dysfunction of liver cells. On the other hand, it has been observed that AST increases in blood not only in liver cell dysfunction but also in ischemic damage of some other tissues (brain, heart, skeletal muscle, kidney). (8, 9)

"De Ritis" ratio is defined as the ratio of serum AST level to ALT level and is a parameter whose relationship with prognosis has been evaluated in different patient groups. An increased De Ritis ratio has been found to be associated with mortality in different patient populations. (10-19)

To the best of our knowledge, this is the first clinical study investigating the relationship between a high De Ritis ratio and GI bleeding mortality.The aim of this study is to investigate the predictors of in-hospital mortality in patients followed up with GI bleeding, and also to search the relationship between the De Ritis ratioand GI bleeding mortality.

METHODS

Records of the patients who had been hospitalized with upper GI bleeding and had been given treatment in the intensive care unit of our hospital between January 2018 and April 2022 were evaluated retrospectively. Patients with lower GI bleeding, younger than 18 years old, or voluntarily discharged from the hospital before their treatment is completed had been excluded from the study. Patients 18 years and older with a definite diagnosis of upper GI bleeding and who completed their treatment in our hospital until discharge or death were included. Upper GI bleeding was defined as: Gastrointestinal hemorrhage that originates proximal to the ligament of Treitz.

Baseline clinical characteristics (gender, age, comorbidities such as hypertension, diabetes mellitus, chronic liver failure, chronic renal insufficiency, neoplastic disease, coronary artery disease, chronic obstructive pulmonary disease, cerebrovascular accident), APACHE score at the time of intensive care unit admission, laboratory parameters on admission (hemoglobin, white blood cell count, platelet count, AST level, ALT level, international nor The primary ratio (INR), albumin level), red blood cell unit transfusion, duration of intensive care unit stay and mortality data were recorded and analyzed.

The primary endpoint was in-hospital mortality and it was defined as mortality that occurred because of upper GI bleeding after diagnosis and during a hospital stay.

The ethical approval was obtained from the ethics committee of the university. The current study was conducted according to the Declaration of Helsinki.

Statistical Analyses: Statistical analyses were performed with SPSS version 22 (SPSS Inc., Chicago, IL, USA). Categorical variables were presented as count and percentage whereas continuous variables with normal distribution were expressed as mean ± standard deviation and continuous variables with abnormal distribution were expressed as median (interquartile range) after examining with the Kolmogorov-Smirnov test. Differences between groups for categorical variables were examined with Chi-squared or Fisher test and differences for continuous variables were examined with Mann Whitney U or Student t test.

Logistic regression analyses were performed to search for the correlation of the current variables with in-hospital mortality.

First, differences between survivor and non-survivor groups were investigated. Then, for further analysis of the De Ritis ratio and its relation with current variables the study population was divided into three equal parts each containing 81 patients. The cut-off point between the second tertile and third tertile was chosen as

a reference point to divide the whole population into two parts named low De Ritis group and high De Ritis group in a similar way to a previous clinical study. (13) P<0.05 was accepted as statistically significant for all analyzes.

RESULTS

A total of 243 patients were enrolled in the study according to the inclusion criteria. The median age of the study population was 68 (16) years and 65.8% were male. The median intensive care unit stay was 2(2) days and the median APACHE score on admission was 17(10) points. The in-hospital mortality rate was 13.1%. Variceal bleeding accounted for 23.1% of all upper GI bleeding. The most encountered comorbid diseases in the study population were hypertension (55.1%), coronary artery disease (40.3%), diabetes mellitus (36.2%), chronic liver failure (22.2%), and chronic renal insufficiency (18.9%).

Comparing survivors and non-survivors in the terms of clinical and laboratory characteristics male gender, variceal bleeding, chronic renal insufficiency, and chronic hepatic failure were more prevalent in non-survivors. While APACHE score, white blood cell count, and INR were higher in non-survivors, albumin level was higher in survivors. (Table 1)

Table 1: Clinical and laboratory characteristics of the survivor and non-survivor patients.

Variables	Survivors (n=211)	Non-survivors (n=32)	P value
Age, years	68 (17.5)	70 (14.75)	0.514
Gender, female/male	77 /134	6 /26	0.049 *
Intensive care unit length of stay, days	2 (2)	2 (3.75)	0.073
Variceal /Nonvariceal bleeding	42 /168	12 /12	0.001*
APACHE score	16 (9)	24 (9.75)	0.000*
Hypertension	118	16	0.530
Diabetes mellitus	76	12	0.871
Coronary artery disease	88	10	0.261
Chronic renal insufficiency	34	12	0.004*
Chronic hepatic failure	42	12	0.026*
Chronic obstructive pulmonary disease	17	6	0.095
Cerebrovascular accident	25	1	0.217
Neoplastic disease	34	6	0.708
Hemoglobin level, g/dL	8.63 ± 2.550	8.92 ±1.956	0.568
White blood cell count, $x10^9$ L	9.7(6.17)	12.75 (9.64)	0.002*
Platelet count, $x10^9$ L	214.0(128.3)	183.4 (98.9)	0.388
Aspartate aminotransferase level, U/L	20 (16)	22.5 (31.75)	0.074
Alanine aminotransferase level, U/L	15 (14)	18.5 (26.5)	0.349
De Ritis ratio	1.27 (0.710)	1.5 (0.675)	0.058
Albumin level, g/dL	3.09 ±0.597	2.49 ±0.569	0.000*
International Normalized Ratio level	1.16 (0.310)	1.43 (0.898)	0.000*
Red blood cell unit transfusion	2 (3)	2(3)	0.582

Categorical variables were given as count; continuous variables were given as mean ±standart deviation with normal distribution and as median (interquartile range) with the abnormal distribution.

Surprisingly, the De Ritis ratio did not show a significant difference between survivors and non-survivors (p=0.058). (Figure 1)

The cut-off point separating low and high De Ritis groups were 1.57. (Figure 2) In parallel with the above-mentioned results variceal bleeding and chronic hepatic failure were more prevalent in the high De Ritis group. Whereas albumin level was higher in the low De Ritis group, ALT, AST, and INR values were higher in the high De Ritis group. The mortality ratio was not statistically significant between these groups.

(Table 2)

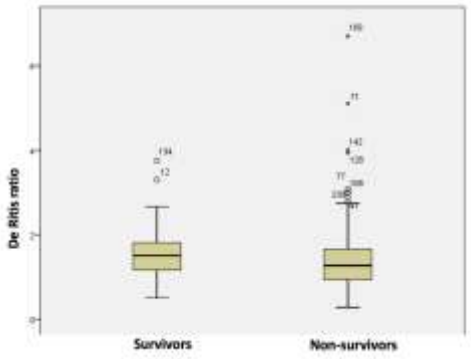

Figure 1: Box plot of the De Ritis ratio in survivors and non-survivors.

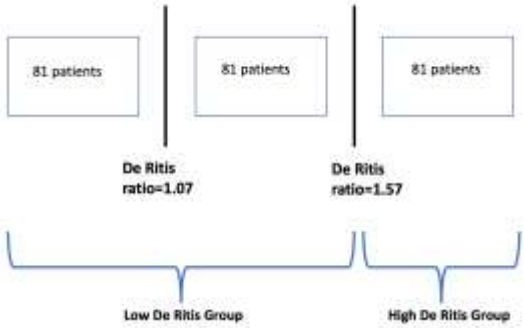

Figure 2: The diagram presents grouping according to the De Ritis ratio.

Table 2: Clinical and laboratory characteristics of the patients grouped by the De ritis ratio.

Variables	De Ritis ratio 1.57 (n=162)	De Ritis ratio ≥ 1.57 (n=81)	P value
Age, years	68 (16)	69.5 (17)	0.067
Gender, male	111	49	0.214
Intensive care unit length of stay, days	2 (2)	2 (2)	0.614
Variceal bleeding	27	27	0.002*
APACHE score	17 (10)	17 (10)	0.067
Hypertension	90	44	0.855
Diabetes mellitus	64	24	0.131
Coronary artery disease	67	31	0.644
Chronic renal insufficiency	28	18	0.354
Chronic hepatic failure	28	26	0.009*
Chronic obstructive pulmonary disease	18	5	0.215
Cerebrovascular accident	17	9	0.883
Neoplastic disease	24	16	0.328
Hemoglobin level, g/dL	8.85 ±2.558	8.36 ±2.298	0.145
White blood cell count, $x10^9$ L	10.370 (6.880)	9.625(6.123)	0.294
Platelet count, $x10^9$ L	217.0 (12.185)	182.5 (13.952)	0.069
Aspartate aminotransferase level, U/L	17 (13)	27 (33)	0.000*
Alanine aminotransferase level, U/L	17 (14)	13 (14)	0.005*
Albumin level, g/dL	3.06 ±0.642	2.88 ±0.580	0.038*
International normalized ratio level	1.14 (0.23)	1.345 (0.54)	0.000*
Red blood cell unit transfusion	2 (3)	2 (3)	0.761
Survivor/Non-survivor	144/18	67/14	0.180

Categorical variables were given as count; continuous variables were given as mean ±standart deviation with normal distribution and as median (interquartile range) with the abnormal distribution.

Logistic regression analyses showed that the risk of mortality increased with a high APACHE score (p=0.000) and the presence of chronic renal insufficiency (p=0.012). On the other hand high albumin level (p=0.007) and having coronary artery disease (0.043) were found to decrease the risk of mortality. The De Ritis ratio was not correlated with mortality risk. (Table 3)

Table 3: Logistic regression analyses showing odds ratios for the current variables.

Variables	OR (95% CI)	P value
Age	0.998 (0.951-1.047)	0.932
Gender, male	0.499 (0.145-1.722)	0.271
Intensive care unit length of stay	0.774 (0.556-1.0779	0.129
APACHE score	0.858 (0.789-0.932)	0.000*
Hypertension	1.026 (0.317-3.319)	0.966
Diabetes mellitus	1.637 (0.523-5.120)	0.397
Coronary artery disease	3.612 (1.042-12.528)	0.043*
Chronic renal insufficiency	0.208 (0.061-0.712)	0.012*
Chronic hepatic failure	1.406 (0.379- 5.215)	0.611
Chronic obstructive pulmonary disease	0.259 (0.057-1.182)	0.081
Cerebrovascular accident	2.644 (0.259-26.973)	0.412
Neoplastic disease	2.221 (0.546-9.035)	0.265
Hemoglobin level	0.787 (0.574-1.077)	0.135
White blood cell count	1.000 (1.000-1.000)	0.596
Platelet count	1.000 (1.000-1.000)	0.715
Aspartate aminotransferase level	0.996 (0.988- 1.003)	0.262
Alanine aminotransferase level	1.008 (0.995-1.022)	0.225
De ritis ratio	0.871 (0.359-2.111)	0.760
Albumin level	3.883 (1.438-10.484)	0.007*
International normalized ratio level	0.963 (0.840-1.103)	0.586
Red blood cell unit transfusion	1.083 (0.715-1.641)	0.706

Abbreviations: CI: Confidence interval, OR: Odds ratio.

DISCUSSION

Based on our results it was determined that the De Ritis ratio did not show a significant difference between survivors and non-survivors of GI bleeding. Variceal bleeding and chronic hepatic failure were more prevalent in the high De Ritis group, albumin level was higher in the low De Ritis group. ALT, AST, and INR values were higher in the high De Ritis group. The mortality ratio was not statistically significant between the high and low De Ritis groups. High albumin levels and having coronary artery disease were found to decrease the risk of mortality. Moreover, the De Ritis ratio was not correlated with mortality risk.

Contrary to our results, the De Ritis ratio was correlated with mortality risk in several studies on various cases and medical conditions. It was found that the De Ritis ratio was a prognostic factor in bladder cancer patients who underwent radical cystectomy (12), its increased levels were associated with in-hospital mortality in COVID 19 patients (13), and it was associated with an increase in critical leg ischemia in patients with peripheral artery disease. (14) A meta-analysis concluded that preoperatively decreased De Ritis ratio in urothelial carcinomas was associated with poor prognosis. (15) It was found that the increased De Ritis ratio at admission in acute ischemic stroke patients had a negative effect on clinical outcomes in the 3rd month. (16) It was concluded that increased De Ritis ratio in oral and oropharyngeal cancer patients affected the prognosis negatively. (17) It was even found to be a strong and independent predictor of long-term mortality after a heart attack (18)

In a study conducted by Wang et al. clinical data of major burn patients admitted between May 1, 2005, and April 30, 2018, were reviewed. (25) In this study, the De Ritis ratio was found to be a new prognostic indicator for major burn patients. Moreover, Yu et al. Reported that the De Ritis ratio was an important predictor to reduce mortality after burn surgery (26). In another study, data from 240 patients were examined and it was concluded that AST/ALT was a prognostic indicator for PLA (27).Polymyositis/dermatomyositis-associated interstitial lung disease ın a cohort study with 522 cases, the De Ritis ratio was associated with increased mortality (28). Lu et al. conducted a study with 374 consecutive adult cardiac arrest (CA) patients and reported that the De-Ritis ratio was significantly associated with ICU mortality and in-hospital mortality after CA (8). In a recent study, laboratory parameters of 322 COVID-19 patients were evaluated and the De Ritis ratio was associated with mortality in these patients (29). In the study of Nem et al, the de Ritis ratio was associated with increased postoperative 90-day mortality after cardiovascular surgery (30). In the studies mentioned above, the cut-off values for the De Ritis, a ratio that predicted prognosis or mortality were different from each other. On the other hand, it is known that the range of the De Ritis ratio can vary between 0.7 and 1.4 in healthy individuals (19).

Since GI bleeding is one of the common but difficult to manage conditions in the emergency department, many studies conducted to determine the predictors of mortality for GI bleeding. Many variables such as higher age, low hemoglobin, higher Child-Pugh Class, re-bleeding within 24 h of admission, higher serum bilirubin, lower systolic blood pressure, hemodynamic instability at presentation, albumin, T score, white blood cell, lactatdehidrogenase, high levels of blood urea nitrogen, creatinine, INR were reported as mortality risk factors for gastrointestinal bleeding (5-7, 31-35). In our study, consistent with the literature, high albumin levels and coronary artery disease were found to decrease the risk of mortality. In many studies, serum albumin concentration is inversely proportional to mortality reported (36). This result supports the decrease in the mortality rate of the high albumin level detected in our study. Moreover, we think that the drop in the mortality risk in patients with coronary artery disease may be due to systemic regulatory effects of anticoagulants and other drugs used for coronary heart disease.In our study, a high APACHE score and the presence of chronic renal insufficiency were found to be associated with increased mortality risk. Many studies have shown that high APACHE scores and organ failure are associated with increased mortality in intensive care unit patients. (37,38) An increased De Ritis ratio has been shown to be an independent predictive factor for mortality in different patient populations. Since there is no previous study researching the relationship between GI bleeding and De Ritis ratio, our related results could not be compared with the literature data.

Limitations: The retrospective nature of patient datawas the most important limitation for our study.The other limitation was the inclusion of data from a single center in our study.

CONCLUSION

Many studies in the literature demonstrated that the De Ritis ratio has prognostic value for different diseases. Our results showed for the first time that the De Ritis ratio was not associated with in-hospital mortality in GI bleeding but further large clinical studies are needed to examine this issue. We think that our results will be a useful reference for different studies investigating the prognostic role of the De Ritis ratio.

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