Original Article

Elevated Bilirubin-to-Albumin Ratio as a Predictor of Mortality in Liver Diseases

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Abstract

Objective: The objective of this study is to evaluate the prognostic accuracy of the bilirubin-to-albumin ratio for predicting mortality in patients with chronic or acute liver disease presenting with acute liver failure.

Methodology: The study duration was about 3 months extending from 10th August 2024 to 22nd December 2024. We consecutively collected 69 patients of both genders with chronic or acute liver diseases presenting with liver failure as evidenced by hepatic encephalopathy, increased prothrombin time and INR. The patients were recruited from the wards and ICUs of the respective hospitals. The underlying etiology of liver disease was identified, and related blood tests including the serum bilirubin and albumen, were performed within the first 24 hours of admission at the main laboratories of the respective hospitals. Bilirubin-to-albumin (B/A) ratio was calculated by dividing the total bilirubin (mg/dl) by the serum albumin (gm/dl) at the time of admission. The normal range of the bilirubin albumen ratio (B/A) is 0.01–0.2, while levels above 0.7 were considered significant and classified as elevated in this study. All patients were monitored throughout their hospital stay and for three months post-discharge. Mortality within this follow-up period was assessed.

Results: The total number of patients was 69 and the age range was from 1 to 62 years with mean age of 43.130±4.90 years and mean duration of liver disease was 19.985±4.55 months. An elevated bilirubin/albumin (B/A) ratio was diagnosed in 29(42%) and the total mortality was seen in 33(47.8%). Bilirubin/Albumin (B/A) ratio showed sensitivity of 66.7%, specificity 80.5%, diagnostic accuracy 74%, with positive predictive value 75.9% and negative predictive value of 72.5%.

Conclusion: Results from the present study showed that a normal or near normal Bilirubin/Albumin (B/A) ratio determined on admission predicts good prognosis regarding the survival of patients with acute liver failure. Based on our preliminary data, a future study with a large number of patients would be required to adequately power a multivariate analysis.

Keywords: Albumin, bilirubin/albumin ratio, bilirubin, liver disease, mortality.

Introduction

Serum bilirubin level is an important biochemical parameter indicating the underlying liver disease. It is a metabolite of heme, which is potentially a toxic substance to the brain, especially in children and neonates. Liver is a huge organ that, through enzymatic mechanisms, conjugates/detoxifies the bilirubin to make it excretable in the bile. High bilirubin level may produce a yellowish tinge in the skin and urine, which can be detected through clinical examination.

There are two main sources of bilirubin in the blood: one is the heme, which results from the breakdown of hemoglobin in aging red blood cells, and the other is myoglobin, which comes from muscle breakdown. The daily bilirubin production in the body is approximately 4 mg per kilogram of body weight.[1] Around 80% of bilirubin production originates from the degradation of hemoglobin in aging red blood cells and prematurely destroyed erythroid cells in the bone marrow. The remaining bilirubin is generated from the turnover of heme-containing proteins in other tissues, primarily the liver and muscles. These proteins include myoglobin, cytochromes, catalase, peroxidase, and tryptophan pyrrolase.[2]

Liver diseases contribute to around 60% of deaths worldwide, with chronic liver disease (CLD) alone accounting for nearly 2 million fatalities each year.[3] CLD is characterized by the loss of the liver parenchyma's regenerative ability due to persistent injurious stimuli, ultimately leading to liver failure. The debilitating consequences of CLD significantly impair quality of life, resulting in increased morbidity and mortality.[4]

A low albumin level is a useful indicator for predicting poor prognosis in acutely ill patients with liver disease.[5] Due to its significance in assessing outcomes for ICU patients, serum albumin level has been incorporated into the Acute Physiology and Chronic Health Evaluation (APACHE) III score.[6]

Other literature has mentioned the significance of low albumin level as an independent risk factor for mortality in seriously ill patients due to liver disease.[7] Some other studies have also assessed the predicting value of albumin to bilirubin ratio for mortality of the patients with liver disease.[8] In another study by Chen B, et al. has shown that Bilirubin/Albumin (B/A) ratio has sensitivity and specificity by 65.9% and 81.4% respectively as a predictor of mortality in chronic liver disease patients,[9] while the overall mortality of acute liver failure is 58% and the prevalence ranges from 35 to 65%.[10]

Though there have been few studies on use of (B/A) ratio as a predictor of mortality in liver disease, such study in our general population as a whole is lacking in our setup. Being simple and just two parameter criteria, we planned this study to assess the accuracy of (B/A) ratio for the predication of mortality in chronic/acute liver disease patients presenting with liver failure taking death within 3 months as a mortality parameter. Though this study was performed in a small number of patients, but provide sufficient ground for performing large scale study on the topic for further elaboration.

Methodology

This was a multicenter descriptive cross-sectional study performed in the Department of Medicine, Hayatabad Medical Complex, Peshawar, Department of Pediatrics, Lady Reading Hospital, Peshawar, and Department of General Medicine, District Headquarters Teaching Hospital, Haripur, Pakistan, from 10th August 2024 to 22nd December 2024. Sixty-nine consecutive patients of acute/chronic liver disease who were admitted in the respective wards for acute liver failure, were collected for the study. Written consent was taken on a preformed Performa from the patient/guardian for including in the study. Ethical approval was taken from the ethical committee Hayatabad medical complex Peshawar with certificate No.1974, Doc No.HMC-QAD-F-00 dated 9th August 2024.

Sample size was calculated with the help of sensitivity and specificity calculator.

Expected sensitivity = 65.9%.

Expected specificity = 81.4%.

Considering the prevalence of acute on chronic liver failure = 35-65%.[10]

Confidence interval = 95%, Precision for sensitivity 15%, for specificity15%

Patients with the following confounding co-morbidities were excluded from the study;

- History of malignancy on medical record
- History of protein loss/hypoalbuminemia (like malnutrition, chronic diarrhea, nephrotic syndrome)
- History of dementia on medical record
- Pregnancy on ultrasound or on medical record
- History of chronic kidney disease on medical record

All patients were subjected to the laboratory tests, serum bilirubin, serum albumen, prothrombin time, liver enzymes and ultrasound abdomen showing cirrhosis or echogenic liver. B/A ratio was calculated taking 0.01 to 0.2 as normal, while more than 0.7 was taken as elevated, the values which has been used in the other study as well.11

The (IBM-SPSS-23) software was used for statistical data analysis. Mean ±SD was calculated for quantitative variables like age and duration of liver disease. Frequency and percentage were computed for qualitative variables like gender. Sensitivity, specificity, Pos-

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itive predictive value, Negative predictive value and diagnostic accuracy for B/A ratio against death was calculated by using 2X2 model. Effect modifiers like age, gender and duration of liver disease were controlled by stratification. Post stratification using diagnostic accuracy was calculated, p value ≤0.05 was considered statistically significant.

We calculated the sensitivity, specificity, positive predictive value and negative predictive value for the B/A ratio as a predictor of mortality using the following formula.

$$\text{Sensitivity} = \frac{a}{a + c} \times 100$$

$$\text{Specificity} = \frac{d}{b + d} \times 100$$

$$\text{Positive Predictive Value} = \frac{a}{a + b} \times 100$$

$$\text{Negative Predictive Value} = \frac{b}{c + d} \times 100$$

$$\text{Diagnostic Accuracy} = \frac{a + d}{a + d + b + c} \times 100$$

a. True positive (Elevated B/A ratio in non-survivors)

b. False positive (Elevated B/A ratio in survivors)

c. False negative (Normal B/A ratio in non-survivors)

d. True negative (Normal B/A ratio in survivors)

Results

Age range in this study was from 1 to 60 years with mean age of 43.130±4.90 years and mean duration of liver disease was 19.985±4.55 months as shown in Table-1.

The patients were predominantly males i.e. 76.8% as indicated in Table-2.

Most of the patients selected were having drug induced liver injury, and liver disease due to viral hepatitis B and C. (Table-3).

B/A ratio was found elevated in 29(42%) and total mortality was seen as 33(47.8%) as shown in Table-4.

B/A ratio showed sensitivity of 66.7%, specificity 80.5%, diagnostic accuracy 74%, positive predictive value 75.9% and negative predictive value by 72.5% for mortality of the patients as calculated from table-4 through the given formulas.

Age, gender and duration of liver disease had no significant impact on the mortality of the study patients (p=0.55, 0.37 & 0.83 respectively)

Chi square = 15.76

P value = 0.0001

Abbreviations:

B/A ratio: Serum Bilirubin to Serum Albumen Ratio

TP = (a) True positive (B/A ratio elevated in non-survivors)

FP = (b) False positive (B/A ratio elevated in survivors)

FN = (c) False negative (B/A ratio normal in non-survivors)

TN = (d) True negative (B/A ratio normal in survivors)

Table 1. Mean +SD of patient's age and duration of illness n=69

Demographics		Range	Mean +SD
1	Age(years)	1-60 years	43.130±4.90
2	Duration of liver disease	2months-23 years	19.985±4.55

Table 2. Percentage and frequency of patients according to gender n=69

Category	No. of Patients	%age
Male	53	76.8%
Female	9	13%
Children	7	10%
Total	69	100%

Table 3. Different causes of liver disease in the study patients

S No.	Cause of liver disease	Number of patients
1	Drug induced liver disease	14.49% (n=10)
2	Acute Viral hepatitis (B &E)	15.9% (n=11)
3	Chronic hepatitis (B & C)	49.27% (n=34)
4	Others	20.28%(n=14) (Dengue & cryptogenic cirrhosis liver)
5	Total	100% (n=69)

Table 4. Showing Association of B/A ratio with Mortality

B/A ratio	Mortality		Total
	Non survivors	Survivors	
Elevated	31.88% (TP) n=22	10.12% (FP) n=7	29 (42%)
Not elevated	15.94% (FN) n=11	42%(TN) n=29	40 (58%)
Total	33 (47.82%)	36 (52.17%)	69 (100%)

Discussion

There are few scoring systems, which are used for evaluating the severity of liver diseases and predicting the prognosis. Child–Pugh score is the most widely used scoring system which is calculated through the values of five parameters, like total bilirubin, serum albumin, prothrombin time, ascites, and hepatic encephalopathy. However, the different amounts of ascites and levels of hepatic encephalopathies make these two parameters highly subjective. Due to this factor, evaluation through this system may reduce the accuracy of this scoring system.[12] The (MELDNa), a modified MELD score includes 4 laboratory variables which are, total bilirubin, international normalizing ratio (INR), creatinine, and sodium concentration which eliminates the subjective factors and is comparatively better risk assessment for severity of liver disease.[13] The MELD score was used in the past for eligibility of patients for liver transplantation, and remained as a good prognostic tool for assessing the three-to-six-month survival in patients with liver failure.[14] The B/A ratio provides just 2 laboratory parameters, albumin and total bilirubin. It has been used to assess the severity of liver dysfunction in patients with hepatocellular carcinoma (HCC).15 In this study, the B/A ratio, also labelled as the albumin/bilirubin ALBI score in some literature, was more frequently abnormal for non-survivors than survivors. It was positively correlated with Child–Pugh and MELD scores in CLD patients. The B/A ratio may therefore be used for predicting the mortality in patients with CLD presenting with liver failure. The B/A ratio showed sensitivity of 66.7%, specificity 80.5%, diagnostic accuracy 74%, positive predictive value 75.9% and negative predictive value of 72.5% in our study. These results are similar to the study of Chen's group, and Chen B, et al. which has shown that albumin/bilirubin ratio has sensitivity and specificity by 65.9% and 81.4% respectively as a predictor of mortality in chronic liver disease patients.[9]

The ALBI score (B/A ratio) demonstrated greater accuracy compared to the Child–Pugh and MELD scores separately, likely due to differences in the stages of liver disease among patients recruited in various studies. The B/A ratio uses only two components, making it simpler and easier to calculate than both the MELD and Child–Pugh scores. Furthermore, combining the B/A ratio and MELD scores offers improved prediction of 3-month mortality compared to using the MELD score alone.

Apart from bilirubin and albumen, there are other biochemical markers which can indicate both liver dysfunction and the extent of liver injury. The B/A ratio uses the bilirubin and albumin levels to reflect insufficient liver function and new liver damage. The usefulness of the B/A ratio has been shown in many studies performed in the patients of hepatocellular carcinoma (HCC).[16-19] A study performed in the patients of chronic liver disease, has found that high levels of bilirubin can predict short-term (1-week) mortality.[20] Since albumin is mainly produced by the liver, the decreased albumin level indicates synthetic dysfunction of the liver and a higher risk of negative outcomes. Higher B/A ratio in CLD patients was due to a decreased serum albumin and increased serum bilirubin levels. Furthermore, we found that a lower serum albumin and higher bilirubin levels were mainly in the non-surviving group compared with the surviving patients. Therefore, the levels of these two important parameters may be used to predict the severity and progression of liver injury in patients with liver disease.

There are several limitations in our study. First, this was a cross sectional study and only one time B/A ratio at the time of admission was used. Second, it could enroll small number of patients in spite of being multicenter, so a large multicenter study will be needed to confirm the findings. Third, the B/A ratio was not serially measured to find out the rate of hepatic functional decline. Therefore, it was not clear whether the B/A ratio is step-wise elevated based on the progressive deterioration of liver function or a rapid decline has occurred during acute liver failure. Furthermore, we used a cut-off for B/A ratio of 0.7 but some studies used lower cut-off values (0.31) in their research,[21] so further studies may be needed to find out an optimum cut-off level for better outcomes.

Conclusion

The findings of this study indicate that the Bilirubin/Albumin (B/A) ratio measured at admission can predict the survival probability of patients with liver disease. This ratio is easily obtained through a simple, non-invasive blood tests and provides an objective assessment. However, further prospective research involving larger, multicenter patient cohorts are necessary to validate the prognostic significance of the B/A ratio in liver diseases.

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Authors' Contribution Statement

NS contributed to the conception, design, acquisition, analysis, interpretation of data, drafting of the manuscript, critical review, and final approval of the version to be published. MH contributed to the design, acquisition, analysis, drafting of the manuscript, and critical review of the manuscript. NM contributed to the acquisition, analysis, interpretation of data, and drafting of the manuscript. SA contributed to the acquisition, analysis, interpretation of data, and drafting of the manuscript. All authors are accountable for their work and ensure the accuracy and integrity of the study.

Conflict of Interest

Authors declared no conflict on interest

Grant Suppport and Financial Disclosure

None

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.