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LETTER TO THE EDITOR

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LETTER TO THE EDITOR

Concomitant determination of hematological indices supported the application of the albumin-bilirubin score in non-malignant liver diseases

Marwan S M Al-Nimer

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Abstract

The albumin-bilirubin (ALBI) score is a useful prognostic marker that predicts mortality in patients suffering from terminal diseases. Recently, it has been reported that ALBI score is a predictor of non-malignant liver diseases. The cutoff point of the ALBI score that distinguishes hepatocellular carcinoma from non-malignant liver disease is still not identified. Therefore, the ALBI score is a sensitive rather than a specific predictor of the poor outcomes of liver diseases. There are many hematological indices and ratios that are utilized as prognostic biomarkers. Among these biomarkers are the neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio (PLR), and platelet-hemoglobin ratio (PHR), which are useful discriminating prognostic biomarkers for liver diseases, *e.g.*, hepatocellular carcinoma, hepatitis, liver fibrosis, *etc.* There is evidence that PLR and PHR are prognostic biomarkers that predict the poor outcomes of diseases. Therefore, concomitant measurements of ALBI score and PHR or ALBI score and PLR will improve the predictive value that can differentiate hepatocellular carcinoma from non-malignant diseases.

Key Words: Albumin-bilirubin score; Hepatocellular carcinoma; Non-malignant diseases; Platelet-lymphocyte ratio; Platelet-hemoglobin ratio

Core Tip: Albumin-bilirubin (ALBI) score is a prognostic biomarker in hepatocellular carcinoma and non-malignant liver diseases, as a higher level in the pretreatment state is associated with poor prognosis. Hematological ratios, notably the platelet-lymphocyte ratio (PLR) and platelet-hemoglobin ratio (PHR) are also useful prognostic biomarkers in hepatic pathological conditions. Concurrent measurement of PLR and ALBI score, or ALBI score and PHR, supports the prediction value of the ALBI score and makes sense to establish a cutoff value for non-malignant conditions.

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TO THE EDITOR

I read with great interest an elegant review (Role of albumin-bilirubin score in non-malignant liver disease) by Xu *et al*[1] who highlighted the useful application of albumin-bilirubin (ALBI) score as a predictor for non-malignant liver disease. I comment on this review by combining the ALBI score with other hematological indices and ratios to improve the predictions of non-malignant liver diseases. Different degrees of liver function degradation are caused by liver disorders, which are also occasionally connected to the inflammatory process. It is therefore quite interesting to combine two biomarkers groups. One of them is the ALBI score, which is represented as a marker of liver function, and the other is the hematological ratios that are utilized as prognostic biomarkers of liver diseases associated with inflammatory processes.

The ALBI score is a useful prognostic tool applicable to liver diseases and surgical or medical interventions used in the management of pathological conditions of the liver[2]. The prognostic value is related to the ALBI grades, which include three grades: Grade 1: ≤ -2.6; Grade 2: -2.60 < and ≤ -1.39; and Grade 3: > -1.39[3]. The grades of ALBI score were related to overall survival and disease-free survival of patients treated with surgery, radiation therapy, or multiple interventions, according to the authors of one meta-analysis study that included 32 clinical studies with a total of 22911 patients with hepatocellular carcinoma. The authors found that a higher ALBI grade is associated with poor overall survival [hazard ratio (HR) = 2.060, 95% confidence interval (95%CI): 1.909-2.211, $P < 0.001$] and early tumor recurrence (HR = 1.264, 95%CI: 1.042–1.485, $P < 0.001$, using multivariate analysis)[4]. In patients undergoing liver transplantation, a different study showed that the grade of the ALBI score is a determinant and significantly associated with the 1- and 5-year survival rates[5]. The ALBI scores were specifically linked to fatal complications of post-transplant graft dysfunction and infection[5]. It has been reported that the ALBI index is one of the nine biomarkers used in the assessment of hepatitis B virus (HBV)-related disease; and a higher score is considered an accurate predictor of mortality within 1 month[6-9]. The ALBI score is a significant predictor of 2-year, 3-year, 4-year, 5-year, and overall causes of mortality in patients with liver cirrhosis associated with chronic hepatitis B; patients with reduced mortality rates had lower ALBL scores[8]. In a retrospective study that included 81 patients with decompensated liver cirrhosis related to HBV, the non-surviving patients within 2 months of follow-up had a significantly higher ALBI score (-0.79) compared with surviving patients (-1.16)[7]. ALBI score (> -2.6) is a predictive biomarker for all-cause mortality for 1, 3, 5, and 10 years in HBV-related disease, as the areas under the curves are 0.816, 0.808, 0.809, and 0.806, respectively[10].

In addition to the albumin and bilirubin levels that are used to determine the ALBI score, other biomarkers are also utilized to evaluate the prognosis of liver disease.

The neutrophil-to-lymphocyte ratio (NLR) is a useful discriminating prognostic biomarker as it is positively and significantly correlated with liver fibrosis in non-alcoholic fatty liver disease, while it is negatively correlated with fibrosis related to HBV but not to hepatitis C virus[11]. It is not a useful discriminating biomarker for liver cirrhosis[12], and a cutoff value of > 2 is a predictor of liver fibrosis[13]. A higher NLR of > 6.12 was reported as a predictor of a worse prognosis in patients with acute or chronic liver failure[14]. Platelet-to-lymphocyte ratio (PLR) is a non-specific predictor of mortality in many diseases[15-19]. In liver diseases, PLR is related to the severity of the disease[20], and it is an accurate discriminating predictor between compensated and decompensated liver cirrhosis resulting from HBV[21]. Furthermore, a higher PLR is a significant predictor of short-term mortality in patients with HBV-related hepatocellular carcinoma who were subjected to surgical intervention[22]. Patients with hepatocellular carcinoma who had a PLR value of < 100 are likely to respond to immunotherapy with a prolonged overall survival compared with those with PLR values > 100[23]. The median value of PLR in non-malignant liver diseases is less than 100, and a significantly higher value was observed in liver fibrosis[24]. Therefore, PLR value is not a useful biomarker to differentiate malignant from non-malignant liver diseases, and a concomitant measurement of PLR and ALBI score could improve the assessment of reserve liver function. The non-specific predictor of both short- and long-term mortality, the platelet-to-hemoglobin ratio (PHR), has not been studied as a prognostic marker in patients with non-liver diseases; instead, it has been studied in patients with other pathological conditions, such as acute pulmonary embolism and congestive heart failure[25–27]. In one study that included 243 patients with locally advanced hepatocellular carcinoma, a PHR of < 1.26 showed a 1-year survival rate of 62.5%, compared with 38.8% in patients with a PHR of > 1.26. In addition, a PHR is associated with other prognostic predictors, *e.g.*, serum albumin and total bilirubin[28]. In addition, both PLR and PHR are elevated in malignancies *e.g.*, carcinoma of the colon, which is associated with tumor size and invasion, and the diagnosis of carcinoma of the colon is improved when it is combined with the other laboratory marker, PHR[29]. Therefore,

concomitant measurement of the PHR and ALBI score could improve the prognostic value in the assessment of hepatic cellular carcinoma as a determinant of the survival rate.

Therefore, the prognosis of liver diseases can be better predicted when hematological ratios, which are indicators of systemic inflammation, are combined with the ALBI score, which determines liver function reserve. This is especially true for conditions like hepatitis or liver fibrosis, where inflammation is a contributing factor to the pathological condition. Concurrently determining these biomarkers may be useful in clinical practice to identify individuals requiring hospital admission and rigorous treatment regimens, as well as to forecast the unfavorable prognosis of the diseases.

It concluded that a combined determination of the ALBI score with NLR or PLR will improve the accuracy of predicting and identifying the patients with poor outcomes, while combining the ALBI score and PHR will improve the accuracy of predicting the poor outcome that is ultimately associated with mortality as it serves as an index of overall survival or disease-free survival. Thus, the accuracy of the prediction of the short- and long-term mortality of non-malignant liver disorders, such as liver fibrosis, will be improved by combining the ALBI score and PHR. To validate these indicators and investigate the possibility of other biomarkers in the evaluation of non-malignant liver diseases, more study is required.

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