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Relationship between Histopathological Stages of Liver and Albumin-Bilirubin Score in Hepatitis B Infection

Hepatit B Enfeksiyonunda Karaciğer Histopatolojik Evreleri ile Albumin-Bilirubin Skoru Arasındaki İlişki

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ABSTRACT

Aim: In this study, sensitivity and specificity of the albumin-bilirubin (ALBI) score were investigated to detect significant liver fibrosis, and these findings were then compared to fibrosis-4 (FIB-4) and aspartate aminotransferase to platelet ratio index (APRI) scores.

Material and Methods: A total of 69 patients were included in the study. Of these patients, 54 (78.3%) were male and 15 (21.7%) were female. Serology, molecular analysis, biochemical parameters, and pathology results of the patients who underwent a liver biopsy due to a chronic hepatitis B virus (HBV) infection, were retrospectively evaluated. ALBI, APRI, and FIB-4 scores were calculated. To predict the fibrosis stage, F≥2 and F≥4, ALBI, APRI, and FIB-4 scores were investigated using the receiver operator characteristic (ROC) curve analysis.

Results: The area under the ROC curve with 95% confidence interval (CI) for the ALBI, APRI, and FIB-4 scores were 0.613 (95% CI: 0.463-0.762, p=0.160), 0.658 (95% CI: 0.513-0.803, p=0.040), and 0.731 (95% CI: 0.570-0.891, p=0.004), respectively, to predict the F≥2, and 0.758 (95% CI: 0.544-0.971, p=0.090), 0.604 (95% CI:0.451-0.757, p=0.490), and 0.923 (95% CI: 0.856-0.990, p=0.005), respectively, in prediction of F≥4. The sensitivity and specificity rates of the ALBI score were 61.1% and 64.7%, respectively, for the cut-off value of -2.81 in predicting F≥2, and 75.0% and 70.8% for the cut-off value of -2.78 in predicting F≥4.

Conclusion: ALBI scores can be used to detect F≥2 in patients with chronic HBV. However, it is not yet clear whether this approach is superior to other non-invasive methods for detecting F≥4.

Keywords: Hepatitis B; chronic; biopsy; fibrosis.

ÖZ

Amaç: Bu çalışmada albümin-bilirubin (ALBI) skorunun belirgin karaciğer fibrozisini saptamada duyarlılık ve özgüllüğü araştırıldı ve bu bulgular fibrozis-4 (FIB-4) ve aspartat aminotransferaz/trombosit oranı indeksi (aspartate aminotransferase to platelet ratio index, APRI) skorları ile karşılaştırıldı.

Gereç ve Yöntemler: Bu çalışmaya toplam 69 hasta dahil edildi. Hastaların 54'ü (%78,3) erkek ve 15'i (%21,7) kadın idi. Kronik hepatit B virüs (HBV) enfeksiyonu nedeniyle karaciğer biyopsi yapılan hastaların seroloji, moleküler analiz, biyokimyasal parametreler ve patoloji sonuçları retrospektif olarak değerlendirildi. ALBI, APRI ve FIB-4 skorları hesaplandı. Fibrozis evresi F≥2 ve F≥4'ü tahmin etmek için ALBI, APRI ve FIB-4 skorları, alıcı işlem karakteristiği (receiver operator characteristic, ROC) eğrisi analizi kullanılarak araştırıldı.

Bulgular: ALBI, APRI ve FIB-4 skorları için F≥2 tahmininde %95 güven aralığı (GA) ile ROC eğrisi altında kalan alan, sırasıyla, 0,613 (%95 GA: 0,463-0,762; p=0,160), 0,658 (%95 GA: 0,513-0,803; p=0.040) ve 0,731(%95 GA: 0,570-0,891; p=0,004) iken F≥4 tahmininde ise sırasıyla, 0,758 (%95 GA: 0,544-0,971; p=0,090), 0,604 (%95 GA: 0,451-0,757; p=0,490) ve 0,923 (%95 GA: 0,856-0,990; p=0,005) idi. ALBI skoru için duyarlılık ve özgüllük değerleri F≥2 tahmininde -2.81 kesim değeri için sırasıyla, %61,1 ve %64,7 iken F≥4 tahmininde -2.78 kesim değeri için sırasıyla, %75,0 ve %70,8 idi.

Sonuç: Kronik HBV'li hastalarda F≥2'yi belirlemek için ALBI skoru kullanılabilir. Ancak, bu yaklaşımın F≥4'ü saptamak için diğer invaziv olmayan yöntemlerden üstün olup olmadığı henüz açık değildir.

Anahtar kelimeler: Hepatit B; kronik; biyopsi; fibrozis.

INTRODUCTION

Hepatitis B virus (HBV) infection remains a global common health problem, despite the effective vaccine and antiviral treatments that are available (1). It is predicted that approximately 257 million people have been chronically infected with HBV worldwide (2). Eastern Asia, Sub-Saharan Africa, and the Pacific Islands have the highest prevalence rates (3,4). The seroprevalence of the global hepatitis B surface antigen (HBsAg) is predicted to be 3.6% (3).

The estimated number of HBV carriers in Turkey is approximately 3.3 million, and the general prevalence of HBV is 4.57% (5). The prevalence ranges from two percent to three percent in the west of Turkey, whereas it ranges from seven percent to eight percent in the east of Turkey (6).

The risk of developing liver cirrhosis, hepatocellular carcinoma (HCC), and hepatic decompensation is high in chronic HBV (7). Cirrhosis develops in more than 40% of patients with chronic HBV if it is left untreated (7,8). The rate of HCC development within ten years in patients with cirrhosis is 30% (9). Monitoring severe fibrosis and/or inflammation in a hepatitis B infection determines both the treatment and the antiviral treatment strategy (10). The stage (≥2) of liver fibrosis in a chronic HBV infection is the main parameter when deciding whether to initiate treatment (11).

The liver biopsy procedure is accepted as the gold-standard method for diagnosing fibrosis and determining its stage (12). However, an insufficient volume of the biopsy sample may decrease the accuracy of the diagnosis (13,14). As well as being an invasive procedure that may harbor several complications, a liver biopsy may result in an incorrect diagnosis in cases of heterogeneous/dyshomogeneous pathology (15).

As many patients object to repeated biopsies during the follow-up to their disease, and there are serious complication problems, such as bleeding due to the biopsy, non-invasive methods have been developed to detect the stage of liver fibrosis (16,17).

The first method is the aspartate aminotransferase to platelet ratio index (APRI), which was used in 2003 by Wai et al. (18) to detect hepatitis C virus (HCV)-related hepatic fibrosis in patients. The second method is the fibrosis-4 (FIB-4) index, which was developed for chronic HCV/HIV coinfections and then validated for other liver diseases (19,20).

The albumin-bilirubin (ALBI) score, which is the subject of this study, is a new method that was developed to predict the severity of poor liver function, as well as the results of patients with acute liver failure (21). Moreover, the prognostic importance of the ALBI scores in patients with primary biliary cirrhosis was also investigated (22). There is a limited amount of studies that evaluate the ALBI score in predicting fibrosis in chronic HBV infections.

In this study, we analyzed the treatment-naive patients who were diagnosed with chronic HBV infections and underwent a liver biopsy at our hospital. We aimed to determine the diagnostic and threshold values of the ALBI score, which is among the non-invasive biochemical markers, in evaluating liver fibrosis in chronic HBV infections and compare it with other non-invasive markers, such as the APRI and FIB-4 scores.

MATERIAL AND METHODS

Study Design

In this study, the serology, molecular analysis, biochemical parameters, and pathology results of the patients who underwent a liver biopsy due to a chronic HBV infection at Gülhane Training and Research Hospital between October 2016 and September 2019 were retrospectively evaluated. The inclusion and exclusion criteria were as follows: 1) HBsAg and HBV-DNA positivity (≥2000 IU/mL) for more than six months; 2) not having received any antiviral treatment; 3) laboratory analyses allowing ALBI, APRI, and FIB-4 scoring on either the same day as the liver biopsy or the day before; 4) not having any other comorbid diseases that affect the liver; and 5) no immunosuppression. Every patient who met the above criteria was included in the study.

Ethical approval for the study was obtained from the Ethics Committee of Non-Interventional Studies at Health Sciences University, Gülhane Training and Research Hospital (Ethics committee number: 2019/19/339).

Serology and Molecular Testing

The serological and molecular analysis of the serum and plasma samples was performed in our microbiology virology laboratory. HBsAg was qualitatively analyzed using the chemiluminescent enzyme immunoassay (CLIA) technique with the Architect HBsAg Reactive Kits (Abbott, Germany) on the Architect i2000SR system (Abbott, Germany) according to the manufacturer's instructions. To detect HBV-DNA, an isolation device (Magnesia 2448 Anatolia Geneworks, Turkey) and HBV-DNA isolation kit (Viral DNA isolation kit, Anatolia Geneworks, Turkey) were used. The PCR mixture, which was prepared with a Real-Time PCR kit (Bosphore HBV Quantification Kit v2, Turkey), was amplified on a Real-Time PCR device (Montania 4896 Anatolia Geneworks, Turkey).

Non-Invasive Markers of Liver Fibrosis

The demographic and biochemical data of the patients included in the study, such as age, platelet count, serum albumin, total bilirubin, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) levels were used. These markers, including the ALBI, APRI, and FIB-4 scores, were calculated based on the following formulas:

ALBI score =

log (bilirubin (mmol/L) x 0.66) - (albumin (g/L) x 0.085).

The ALBI scores one, two, and three were defined as values less than -2.60, between -2.60 and -1.39, and more than -1.39, respectively (21).

APRI score =

AST (normal upper limit) / platelet (10^9/L) x 100 (18).

FIB-4 Index =

age x AST (U/L) / (platelet (10^9/L) x ALT (U/L)$^{1/2}$) (23).

Histopathological Examination

The patients' liver needle biopsy pathology results, which were obtained from the Department of Pathology's archives, were re-evaluated. The chronic hepatitis activity level and fibrosis stage that were detected in the microscopic examination, performed with preparations with histochemical Hematoxylin Eosin and Masson Trichrome stains, and were stated in the pathology report, were recorded as histopathological data. Ishak modified hepatitis activity index (mHAI) grading and staging system was used to grade chronic hepatitis and stage fibrosis. In this scoring system, the activity level range is

between 0-18, and the fibrosis stages are between 0-6. The mHAI (0-18), which represents necroinflammatory activity, includes the piecemeal necrosis score (0-4), confluent necrosis score (0-6), focal lytic necrosis, apoptosis, and focal inflammation score (0-4), and portal inflammation score (0-4). F0-F1 is accepted as the absence of fibrosis or mild fibrosis, F4-F6 is accepted as severe or significant fibrosis, and F5-F6 is accepted as cirrhosis (24). In this study, the pathological fibrosis scores were defined as follows: F≥2=F2-F6 and F≥4=F4-F6.

Statistical Analysis

Data that was obtained in the study was statistically evaluated using the IBM SPSS v.25 (SPSS Inc, Chicago, IL, USA) package software. To examine whether the variables were normally distributed, they were analyzed using visual methods (histogram and probability plots) and the Kolmogorov-Smirnov test. During the statistical evaluation of the data, descriptive statistics, median, interquartile range (IQR), minimum-maximum, number, and percentage were used. The numerical variables were compared with the Mann-Whitney U or Kruskal-Wallis tests, and categorical variables were analyzed using the chi-square test. To predict the F≥2 and F≥4, the ALBI score, APRI, and FIB-4 indices were investigated using the receiver operator characteristic (ROC) curve analysis. Histology of the liver biopsy was accepted as the gold-standard diagnostic method, and the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (+LR), negative likelihood ratio (-LR), and the accuracy rates of the optimal cut-off values in fibrosis prediction of ALBI, APRI, and FIB-4 were calculated according to the standard formulas. The confidence interval (CI) was determined as 95% in all the statistical evaluations. A p value of less than 0.05 was accepted as statistically significant.

RESULTS

A total of 69 patients between the ages of 13 and 68 years were included in the study. Out of 69 patients, 54 (78.3%) were male and 15 (21.7%) were female. There were only two patients under the age of 18: two female patients aged 13 and 15 years. The median age of the patients was 30 (IQR, 21-48; range, 13-68) years, and the male patients were younger than the female patients, with the median age of 23 (IQR, 21-45; range, 16-64) years vs. 45 (IQR, 39-55; range, 13-68) years (p=0.006). Other demographic and clinical data during the liver biopsy, such as gender, age, albumin, AST, ALT, total bilirubin, and platelet counts were shown in Table 1.

Liver biopsy scores of 26.1% (n=18) of the patients were F≥2. The rates of patients with a histopathological activity index (HAI) score of <5, 5-9 and >9 were 53.6% (n=37), 40.6% (n=28), and 5.8% (n=4), respectively.

The area under the ROC curve (AUROC) values of ALBI, APRI, and FIB-4 for the diagnosis of F≥2 and F≥4 were 0.613 (95% CI: 0.463-0.762, p=0.160) and 0.758 (95% CI: 0.544-0.971, p=0.090); 0.658 (95% CI: 0.513-0.803, p=0.040) and 0.604 (95% CI: 0.451-0.757, p=0.490); and 0.731 (95% CI: 0.570-0.891, p=0.004) and 0.923 (95% CI: 0.856-0.990, p=0.005), respectively. The optimal cut-off values of ALBI, APRI, and FIB-4 for the diagnosis of F≥2 and F≥4 were -2.81 and -2.78; 0.35 and 0.37; and 1.11 and 1.18, respectively. The ROC curves of the ALBI, APRI, and FIB-4 performances in predicting F≥2 and F≥4 were shown in Figure 1, and the optimal cut-off values, sensitivity, specificity, PPV and NPV for the cut-off values in predicting F≥2 and F≥4 were shown in Table 2.

The AUROC values of ALBI, APRI, and FIB-4 for the diagnosis of HAI≥5 were 0.513 (95% CI: 0.375-0.651, p=0.857), 0.721 (95% CI: 0.601-0.841, p=0.002), and 0.598 (95% CI: 0.457-0.739, p=0.163), respectively. The optimal cut-off values of ALBI, APRI, and FIB-4 for the diagnosis of HAI≥5 were -2.98, 0.44, and 1.00, respectively. The ROC curves of the ALBI, APRI, and FIB-4 performances in predicting HAI≥5 were shown in Figure 2, and the optimal cut-off values, sensitivity, specificity, PPV, and NPV for the cut-off values in predicting HAI≥5 were shown in Table 3.

The median value of the HBV-DNA viral load in the 69 patients who were included in the study was $1.5x10^4$ IU/ml (IQR, $2.5x10^3$ - $2.8x10^7$, range, 8 - $5x10^9$). The median value of the HBV-DNA viral load was $1.2x10^4$ IU/ml (IQR, $2.5x10^3$ - $4x10^6$, range, $1x10^2$ - $6.9x10^9$) in F<2 and $1.7x10^6$ IU/ml (IQR, $1.5x10^4$ - $2x10^8$, range, 8 - $5x10^9$) in F≥2 (p=0.020).

The median value of the APRI was 0.35 (IQR, 0.24-0.57, range, 0.1-3.1) in F<2, and 0.51 (IQR, 0.34-0.90, range, 0.2-4.6) in F≥2 (p=0.040). The median value of APRI was 0.29 (IQR, 0.22-0.56, range, 0.1-0.8) in HAI<5, 0.49 (IQR, 0.32-0.59, range, 0.2-3.1) in HAI:5-9, and 1.73 (IQR, 0.83-3.97, range, 0.6-4.6) in HAI>9 (p=0.001).

Table 1. Basic characteristics of the patients who underwent liver biopsy due to hepatitis B infection

Fibrosis Staging	F0	F1	F2	F3	F4	F6	Total
Patient number, n (%)	30 (43.5)	21 (30.4)	6 (8.7)	8 (11.6)	3 (4.3)	1 (1.4)	69 (100)
Gender, n (%)							
Male	23 (76.7)	16 (76.2)	5 (83.3)	7 (87.5)	2 (66.7)	1 (100)	54 (78.3)
Female	7 (23.3)	5 (23.8)	1 (16.7)	1 (12.5)	1 (33.3)	0 (0.0)	15 (21.7)
Age (year)	27 (22-44)	28 (20-47)	32.5 (20-57)	34.5 (21-58)	48 (42-56)	53	30 (21-48)
Albumin (g/L)	42 (38-45)	43 (41-44)	41 (37-43)	41 (38-43)	41 (34-43)	37	42 (39-42)
AST (U/L)	26 (22-49)	38 (24-60)	54 (22-213)	48 (32-128)	35 (31-35)	40	35 (23-55)
ALT (U/L)	33 (22-65)	66 (28-105)	145 (21-218)	66 (26-218)	28 (22-37)	46	46 (24-103)
Total bilirubin (µmol/L)	10.3 (6.9-15.5)	10.3 (8.6-16.3)	8.6 (4.6-17.2)	9.5 (5.2-17.6)	15.5 (10.3-18.1)	29.2	10.3 (6.9-15.5)
Platelet count (10^9/L)	228 (201-272)	232 (194-258)	253 (202-294)	229 (186-311)	174 (135-190)	263	229 (197-271)

AST: aspartate aminotransferase, ALT: alanine aminotransferase, descriptive statistics were presented as the median (25^{th}-75^{th} percentile)

Table 2. ROC analysis results of ALBI score, APRI, and FIB-4 index in predicting Ishak fibrosis stage in patients with HBV

	Cut-off	AUROC	95%CI	p	Sn	Sp	PPV	NPV	+LR	-LR	Accuracy
ALBI											
F≥2	-2.81	0.613	0.463-0.762	0.160	61.1	64.7	37.9	82.5	1.73	0.60	63.8
F≥4	-2.78	0.758	0.544-0.971	0.090	75.0	70.8	13.6	97.9	2.57	0.35	71.0
APRI											
F≥2	0.35	0.658	0.513-0.803	**0.040**	77.8	51.0	35.9	86.7	1.59	0.44	58.0
F≥4	0.37	0.604	0.451-0.757	0.490	100	49.2	10.8	100	1.97	0	52.2
FIB-4											
F≥2	1.11	0.731	0.570-0.891	**0.004**	61.1	90.2	68.8	86.8	6.23	0.43	82.6
F≥4	1.18	0.923	0.856-0.990	**0.005**	100	87.7	33.3	100	8.13	0	88.4

ROC: receiver operator characteristics, ALBI: albumin-bilirubin, APRI: aspartate aminotransferase to platelet ratio index, FIB-4: fibrosis-4, HBV: hepatitis B virus, AUROC: area under the ROC curve, CI: confidence interval, Sn: sensitivity, Sp: specificity, PPV: positive predictive value, NPV: negative predictive value; +LR: positive likelihood ratio, -LR: negative likelihood ratio

Table 3. ROC analysis results of ALBI score, APRI, and FIB-4 index in predicting HAI≥5 grade in patients with HBV

	Cut-off	AUROC	95%CI	p	Sn	Sp	PPV	NPV	+LR	-LR	Accuracy
ALBI	-2.98	0.513	0.375-0.651	0.857	65.6	37.8	47.7	56.0	1.06	0.91	50.7
APRI	0.44	0.721	0.601-0.841	**0.002**	62.5	70.3	64.5	68.4	2.10	0.53	66.7
FIB-4	1.00	0.598	0.457-0.739	0.163	46.9	81.1	68.2	63.8	2.48	0.66	65.2

ROC: receiver operator characteristics, ALBI: albumin-bilirubin, APRI: aspartate aminotransferase to platelet ratio index, FIB-4: fibrosis-4, HBV: hepatitis B virus, AUROC: area under the ROC curve, CI: confidence interval, Sn: sensitivity, Sp: specificity, PPV: positive predictive value, NPV: negative predictive value; +LR: positive likelihood ratio, -LR: negative likelihood ratio

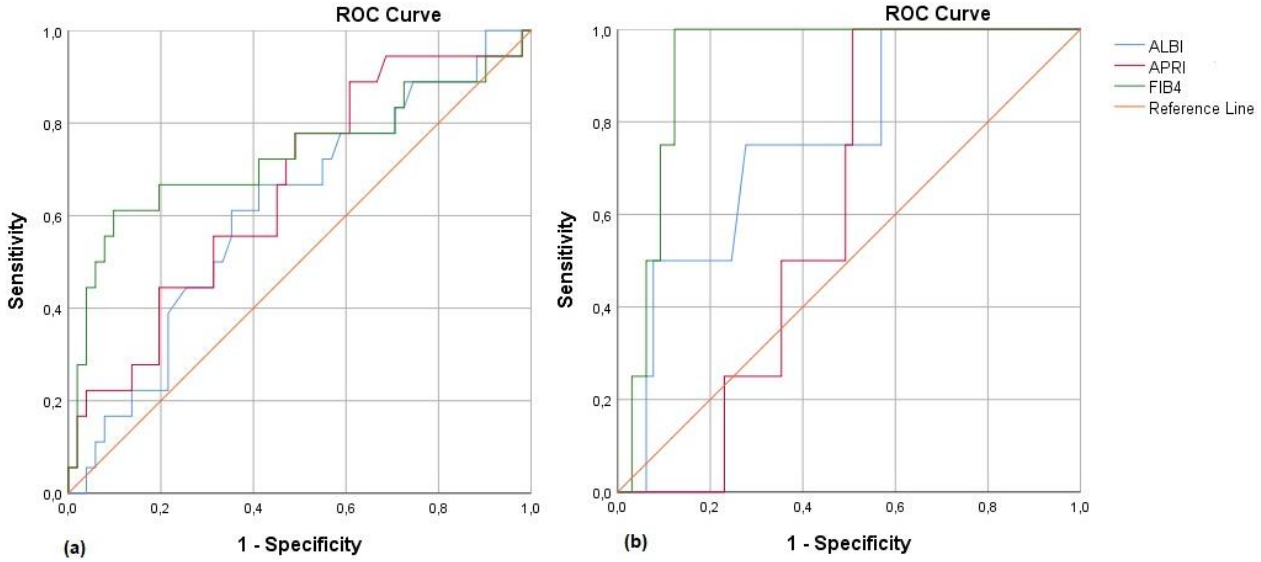

Figure 1. Evaluation of ALBI score, APRI, and FIB-4 index performances in prediction of fibrosis stage **a)** F≥2, **b)** F≥4
ROC: receiver operator characteristics, ALBI: albumin-bilirubin, APRI: aspartate aminotransferase to platelet ratio index, FIB-4: fibrosis-4

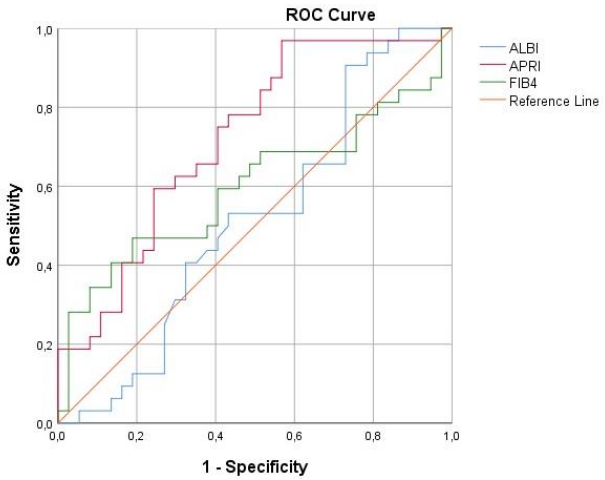

Figure 2. Evaluation of ALBI score, APRI, and FIB-4 index performances in prediction of HAI≥5
ROC: receiver operator characteristics, ALBI: albumin-bilirubin, APRI: aspartate aminotransferase to platelet ratio index, FIB-4: fibrosis-4, HAI: hepatitis activity index

The median value of FIB-4 was 0.65 (IQR, 0.44-0.99, range, 0.0-3.4) in F<2 and 1.18 (IQR, 0.70-1.63, range, 0.2-4.4) in F≥2. The median value of FIB-4 was higher in patients with F≥2, and the difference was statistically significant (p=0.004). The median value of FIB-4 was 0.55 (IQR, 0.44-0.99, range, 0.0-3.4) in HAI<5, 0.80 (IQR, 0.43-1.23, range, 0.2-2.8) in HAI:5-9, and 1.39 (IQR, 0.98-3.71, range, 0.8-4.4) in HAI>9. The FIB-4 index was significantly different in patients with HAI>9 (p=0.040).

The median value of ALBI was -2.91 (IQR, -3.17 to -2.61, range, -3.5 to 0.6) in HAI<5, -2.96 (IQR, -3.10 to -2.71, range, -3.3 to 0.5) in HAI:5-9, and -2.66 (IQR, -2.83 to -2.33, range, -2.9 to -2.2) in HAI>9. No significant difference was found in terms of the ALBI median values among the HAI groups (p=0.210). The median value of ALBI was -2.93 (IQR, -3.10 to -2.70, range, -3.5 to 0.6) in F<2 and -2.77 (IQR, -3.0 to -2.63, range, -3.3 to 0.5) in F≥2 (p=0.160).

DISCUSSION

Detecting the stages of liver fibrosis is important for determining the prognosis of chronic liver disease, choosing the specific treatment for the patient, and to follow-up on the success of the treatment (25). For the last 50 years, liver biopsy as an invasive method has been accepted as the gold standard in liver fibrosis staging (26). Non-invasive alternative methods have been investigated as an alternative to invasive procedures in detecting liver fibrosis (27). Serum tests, proteomic profiles/genetic tests, and imaging techniques are invasive methods that are used in the assessment of fibrosis. The advantages of these techniques are that they are less invasive, there is a low risk of sampling fault and relatively high inter-observer variability/variation, and the measurements can be repeated. Therefore, they allow fibrosis to be continuously followed-up (28).

In this study, ALBI, APRI, and FIB-4 scores had similar diagnostic values for the patients with F≥2 of chronic HBV. However, we found that FIB-4 was better for detection in patients with severe fibrosis or cirrhosis. APRI had a higher diagnostic value for detection in patients with HAI≥5 compared to ALBI and FIB-4.

The first non-invasive method is the APRI score, which was identified in patients with chronic hepatitis C by Wai et al. (18). It is calculated using the AST value and platelet count. It is known that AST levels increase and platelet counts decrease in advanced liver fibrosis. Although platelet production reduces due to the reduced thrombopoietin production by hepatocytes, the platelets are sequestrated in the spleen due to the liver fibrosis progression and the developing portal hypertension. Although the release of AST from mitochondrion increases with liver injury, it reduces fibrosis clearance (30). In this study, the median platelet count was determined as $229x10^9$/L, whereas it was detected as $253x10^9$/L for F2, $229x10^9$/L for F3, and $174x10^9$/L for F4. The platelet count for F4 was below the mean platelet count. The median value of the serum AST levels was recorded as 35 U/L. Although the AST levels for F2 and F3 were 54 and 48 U/L, respectively, the level for F4 was recorded as 35 U/L. This was lower than the others but had the same median value. This was due to the low number of patients with advanced fibrosis, as there were 14 patients for F2 and F3, but only three patients for F4 in the study.

APRI score can be used for diagnostic purposes for both significant fibrosis and cirrhosis. In our study, there was a significant difference in terms of the APRI score according to the presence of fibrosis. The AUROC values in patients with chronic HBV were 0.658 and 0.604 in F≥2 and F≥4, respectively. The cut-off value with the highest rates of sensitivity and specificity was 0.35 for F≥2 (sensitivity, 77.8%; specificity, 51.0%) and 0.37 for F≥4 (sensitivity, 100%; specificity, 49.2%). The AUROC value of the APRI scores in this study was lower than the value, 0.80, that was found by Wai et al. (18). In other studies on patients with chronic HBV, the AUROC values ranged from 0.639 to 0.878 (31-33). Although our results were consistent with the studies in the literature, the low AUROC value that we found may be associated with the low number of patients that were included in the study, as well as the patient group, which consisted of young patients without significant fibrosis. In this study, although the sensitivity of the APRI score increased in advanced stages of fibrosis, the specificity was low, which reveals that APRI cannot replace the gold-standard method of a liver biopsy in assessing the presence and stage of liver fibrosis.

FIB-4 is another non-invasive marker. It is formulated with age, ALT and AST levels, and the platelet count. Like APRI, the FIB-4 values differ due to the increased AST/ALT ratio and reduced platelet count, which is caused by liver fibrosis. In our study, the AUROC value was 0.731 for F≥2 and 0.923 for F≥4. A statistically significant difference was found in the FIB-4 score according to the presence of fibrosis. The cut-off value with the highest rates of sensitivity and specificity was 1.11 for F≥2 (sensitivity, 61.1%; specificity, 90.2%) and 1.18 for F≥4 (sensitivity, 100%; specificity, 87.7%). Our results were similar to the results of other studies in the literature. In the other studies, the AUROC value of FIB-4 was ranged from 0.646 to 0.812 for F≥2, and from 0.715 to 0.818 for F≥4 (31-34). In our study, the FIB-4 score was more successful than the other non-invasive methods, APRI and ALBI, in terms of detecting the presence of significant fibrosis in patients with chronic HBV.

ALBI score was first developed to predict the prognosis of patients with cirrhosis with or without liver cancer (16). Therefore, it is a new model that uses serum albumin and bilirubin to assess the severity of liver function (35). It has a more significant performance compared to the Child-Pugh and MELD scores when predicting the long-term survival rate for patients with HBV-related cirrhosis (33). The number of studies that show a correlation between fibrosis and ALBI in patients with chronic HBV is quite low. In one study, which included 217 patients with chronic HBV, the AUROC value of the ALBI score was 0.698 for F≥2, and 0.843 for F≥4. The sensitivity and specificity rates in the cut-off value of >-2.7 were 42.6% and 91% for F≥2, and 70.45% and 86.13% for F≥4, respectively (36). In another study, which included 91 patients with chronic HBV, although the AUROC value of the ALBI score for fibrosis prediction was 0.849, the sensitivity and specificity rates in the cut-off value of -2.19 in distinguishing cirrhotic and non-cirrhotic cases were 85.7% and 74%, respectively (16). In this study, the AUROC values for F≥2 and F≥4 were 0.613 and 0.758, respectively. Although sensitivity was 61.1% and specificity was 64.7% for F≥2 in the cut-off value of -2.81, sensitivity was 75.0% and specificity was 72.3% for F≥4 in the cut-off value of -2.78. The results were similar to the results of other studies in the literature (16,36). Our study is important as it is one of the rare studies where the ALBI score results are assessed to predict fibrosis in patients with chronic HBV. However, this study has several limitations. The major limitation is that the number of patients is not high enough to obtain general data; either the data or the studies should be multicenter, in addition to including a high number of patients, in order to represent measured the general population. The second limitation is that the ALBI scores could not be dynamically. For this reason, a relationship between the dynamic scores and the transition between the liver function and fibrosis stages and ALBI scores could not be established.

CONCLUSION

In conclusion, it was found that the ALBI score was a prediction index that can be subjectively evaluated, easily reached, and calculated using a non-invasive blood test. Additionally, the ALBI score can be used to detect the absence or presence of fibrosis, especially in patients with chronic HBV. However, although non-invasive methods, such as the ALBI score, cannot replace a liver biopsy, multicenter cohort studies with a high number of samples and studies where more reliable results can be obtained using standardization are needed.

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