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BRIEF ARTICLE

Noninvasive assessment of liver damage in chronic hepatitis B

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Abstract

AIM: To evaluate the efficacy of the aspartate aminotransferase/platelet ratio index (APRI) and neutrophil-lymphocyte (N/L) ratio to predict liver damage in chronic hepatitis B (CHB).

METHODS: We analyzed 89 patients diagnosed with CHB by percutaneous liver biopsy and 43 healthy subjects. Liver biopsy materials were stained with hematoxylin-eosin and Masson's trichrome. Patients' fibrosis scores and histological activity index (HAI) were calculated according to the Ishak scoring system. Fibrosis score was recognized as follows: F0-1 No /early-stage fibrosis, F2-6 significant fibrosis, F0-4 non-cirrhotic and F5-6 cirrhotic. Significant liver fibrosis was defined as an Ishak score of $\geqslant$ 2. APRI and N/L ratio calculation was made by blood test results.

RESULTS: The hepatitis B and control group showed no difference in N/L ratios while there was a significant difference in terms of APRI scores ($P < 0.001$). Multiple logistic regression analysis revealed that the only independent predictive factor for liver fibrosis in CHB was platelet count. APRI score was significantly higher in cirrhotic patients than in non-cirrhotic patients. However, this significance was not confirmed by multiple logistic regression analysis. The optimum APRI score cut-off point to identify patients with cirrhosis was 1.01 with sensitivity, specificity, positive predictive value and negative predictive value of 62% (36%-86%), 74% (62%-83%), 29% (13%-49%) and 92% (82%-97%), respectively. In addition, correlation analyses revealed that N/L ratio has a negative and significant relationship with HAI ($r = -0.218$, $P = 0.041$).

CONCLUSION: N/L ratio was negatively correlated with HAI. APRI score may be useful to exclude cirrhosis in CHB patients.

Key words: Chronic hepatitis B; Fibrosis; Liver cirrhosis; Noninvasive; Serum markers

Core tip: Due to the limitations of liver biopsy, the use of non-invasive markers has emerged in recent years. The aspartate aminotransferase/platelet ratio index (APRI) is used to determine chronic hepatitis C patients with advanced fibrosis. Neutrophil-lymphocyte (N/L) ratio is higher in patients with advanced fibrosis and considered as a novel non-invasive marker to pre-

dict advanced disease in non-alcoholic steatohepatitis. This study showed that N/L ratio is negatively correlated with HAI in chronic hepatitis B (CHB). APRI score may be useful to exclude cirrhosis in CHB patients.

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INTRODUCTION

Hepatitis B virus (HBV) infection is a major health problem all over the world, and is thought to affect 350-400 million people. Disease can be found in a wide range from inactive carrier state to cirrhosis and hepatocellular carcinoma (HCC)[1]. Disease morbidity and mortality in chronic hepatitis B (CHB) depends on the continuation of viral replication and progression of the disease to cirrhosis and HCC[2]. The goal of treatment is to prevent progression of the disease to advanced stages like cirrhosis and HCC. Establishing the status of hepatic fibrosis is important to decide the treatment[2]. Liver biopsy gives more accurate results about liver damage and fibrosis stage. Low patient compliance because of the invasive nature of liver biopsy, the occurrence of bleeding and pain, as a result of faulty sampling and missing pathological evaluation, differences between pathologists in the evaluation of biopsies and the limited use of biopsy in the monitoring of treatment are the limitations of liver biopsy[3,4]. For these reasons, non-invasive tests are needed to determine liver damage and fibrosis in CHB.

The aspartate aminotransferase/platelet ratio index (APRI) has been used to determine chronic hepatitis C (CHC) patients with advanced fibrosis[5]. APRI also predicts significant fibrosis in CHB[6]. The neutrophil-lymphocyte (N/L) ratio can be calculated easily from complete blood counts and is an easily accessible marker which indicates the state of inflammation in the body. It is considered to evaluate disease prognosis in HCC[7,8]. Alkhouri *et al*[9] found that the N/L ratio is higher in patients with non-alcoholic steatohepatitis (NASH) and advanced fibrosis. They also suggested that the N/L ratio can be used as a novel non-invasive marker to predict advanced disease in NASH. In our study, we evaluated APRI and the N/L ratio, which are cheap and easily accessible markers, to determine hepatic damage and fibrosis in patients with CHB. This study aimed to evaluate the efficacy of the N/L ratio to predict significant fibrosis in CHB for the first time in the literature.

MATERIALS AND METHODS

Study population

This study was conducted between January 2007 and November 2008 at Erciyes University Medical Faculty in the Department of Gastroenterology. We retrospectively analyzed 89 patients diagnosed with CHB by percutaneous liver biopsy. Inclusion criteria were accepted as follows: positive surface antigen of HBV for at least 6 months, HBV DNA $\geqslant$ 2.000 IU/mL, patients with pre-treatment liver biopsies, the lack of HIV, HCV and hepatitis D virus infections, the lack of other liver diseases, lack of HCC and lack of alcohol use. The control group consisted of 43 individuals with normal liver tests without systemic disease. All cases were evaluated for clinical and medical background. Our study was conducted in accordance with the principles of the Helsinki Declaration. Erciyes University's Medical Faculty Ethics Committee approved the study.

Calculation of indirect fibrosis markers

APRI and N/L ratio calculation is made by blood test results at least 1 mo prior to liver biopsy. The APRI score was calculated with the formula (AST/40)/platelet (10^9/L) $\times$ 100[5]. The N/L ratio was calculated using the values of neutrophils and lymphocytes obtained from the patients complete blood counts.

Histopathological assessment

Liver biopsy materials were stained with hematoxylin-eosin and Masson's trichrome. All of the liver biopsies were examined by experienced pathologists. Patients' fibrosis scores and histological activity index (HAI) were calculated according to the Ishak scoring system[10]. Fibrosis score was recognized as follows: F0-1 No/early-stage fibrosis, F2-6 significant fibrosis, F0-4 non-cirrhotic and F5-6 cirrhotic. Significant liver fibrosis was defined as an Ishak score of $\geqslant$ 2. This score is also defined as a histologic indication of treatment[11].

Statistical analysis

MedCalc (Version 9.2.0.1) and IBM SPSS Statistics 20.0 (SPSS Inc., Chicago, IL, United States) softwares were used for all analyses. The Shapiro-Wilk's test was used and histogram and q-q plots were examined to assess the data normality. Accordingly, either an independent samples *t* test or Mann-Whitney *U* tests were used to compare the differences of continuous variables between groups. χ^2 analyses were used to compare the differences of categorical variables. Results are expressed as frequencies and percentages, mean ± SD or median (25^{th} and 75^{th} percentiles). Moreover, univariate and multivariate logistic regression analyses were performed and ORs with 95%CI were calculated in order to indentify the risk factors of significant fibrosis and cirrhosis. Significant variables at a $P < 0.10$ level in univariate analysis were taken to multivariate analysis and backward stepwise elimination was used at a $P < 0.10$ stringency level to identify the independent risk factors of significant fibrosis and cirrhosis. Receiver operating characteristic (ROC) curves were plotted for the N-L ratio and APRI score to detect significant fibrosis and cirrhosis. The areas also, cut-offs were determined for each variable. Sensitivity, specifity, positive predictive rate, negative predictive rate and accuracy rate diagnostic measures were calculated and Kappa

Table 1 Comparison of clinical and laboratory parameters between control and hepatitis B patients groups

Variable	Control (n = 43)	Hepatitis B patients (n = 89)	P value
Gender (female/male)	31 (72.1)/12 (27.9)	39 (43.8)/50 (56.2)	0.004
Age (yr)	35.4 ± 12.64	41.5 ±1 3.02	0.012
Platelet count (10^3 μL)	272.0 (242-342)	179.0 (147-231)	< 0.001
Total bilirubin (mg/dL)	0.6 (0.4-0.8)	0.8 (0.6-1)	0.009
AST (IU/L)	17.0 (14-20)	45.0 (30-68)	< 0.001
ALT (IU/L)	16.0 (11-19)	56.0 (36-111)	< 0.001
AP (IU/L)	69.0 (53-79)	72.0 (61-90)	0.086
GGT (IU/L)	17.0 (14-27)	29.0 (21-50)	< 0.001
Neutrophil count	4.3 (3.4-4.9)	3.4 (2.9-4.7)	0.004
Lymphocyte count	2.1 (1.6-2.4)	2.0 (1.6-2.4)	0.355
N/L	2.1 (1.5-2.8)	1.9 (1.4-2.3)	0.123
APRI score	0.1 (0.1-0.1)	0.6 (0.3-1.1)	< 0.001

Values are expressed as n (%), mean ± SD or median (25^{th}-75^{th} percentiles). AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; AP: Alkaline phosphatase; GGT: Gamma glutamyl transferase; N/L: Neutrophil-lymphocyte ratio; APRI: Aspartate aminotransferase/platelet ratio index.

tests were performed for the N/L ratio and APRI score for the given cut-off value. Speaman's rank test was used for correlation analysis. A $P < 0.05$ probability level was considered statistically significant.

RESULTS

In this study 89 patients with hepatitis B and 43 healthy subjects with no systemic disease were included as a control group. There were 31 (72%) females and 12 (28%) males in the control group and also 39 (44%) females and 50 (56%) males in the patient group. The demographic and laboratory data of the hepatitis B and control group are summarized in Table 1.

The hepatitis B and control group showed no difference in N/L ratios while there was a significant difference in terms of APRI scores ($P < 0.001$). In addition, as expected, platelet count, AST, ALT and GGT values were significantly different from those of the control group ($P < 0.001$). While platelet count was lower, AST, ALT and GGT levels were higher in the patient group (Table 1).

In CHB patients, when significant fibrosis was compared with early-stage fibrosis, a significant difference in platelet count and INR values was found ($P < 0.05$). Multiple logistic regression analysis revealed that the only independent predictive factor for liver fibrosis in CHB was platelet count. The APRI score was found to be higher in CHB with significant fibrosis but this increase was not found to be statistically significant (Table 2).

Cirrhotic patients were found to be more elderly compared to the non-cirrhotic patients ($P < 0.05$). The APRI score was significantly higher in cirrhotic patients than in non-cirrhotic patients ($P < 0.05$). However, this significance was not confirmed by multiple logistic regression analysis (Table 3).

ROC curve analysis suggested that the optimum APRI score cut-off point to identify patients with cirrhosis was 1.01 with sensitivity, specificity, positive predictive value and negative predictive value of 62% (36%-86%), 74% (62%-83%), 29% (13-49) and 92% (82-97) respectively (Figure 1, Table 4). In general, the accuracy of the APRI score to determine patients with cirrhosis is 72%. In addition, correlation analyses revealed that the N/L ratio has a negative and significant relationship with HAI (r = -0.218, P = 0.041).

DISCUSSION

In CHB patients with cirrhosis the APRI score was significantly higher but this significance was not confirmed by multiple logistic regression analysis. The APRI score was higher in significant fibrosis but it was not statistically significant. While the N/L ratio was not related with significant fibrosis and cirrhosis, it was found to be negatively correlated with HAI in patients with CHB.

Liver biopsy may give valuable data to assess liver histology in CHB disease

Due to the limitations of liver biopsy, the use of non-invasive markers has emerged in recent years[12,13]. In these studies, positive results were obtained with Fibrotest and Fibroscan to determine advanced fibrosis and cirrhosis in patients with CHB and CHC. Studies have conflicting results with regard to the use of APRI score to predict significant fibrosis in CHB patients. In their study Wai *et al*[14] suggest that APRI score, which is used to predict significant fibrosis and cirrhosis in CHC, was not suitable for patients with CHB. They explain this by the presence of a fluctuating course with acute attacks in CHB patients while the progression of fibrosis in CHC is more quiet. Yilmaz *et al*[15] also confirmed this and concluded that in patients with CHC the APRI score showed good accuracy for the assessment of liver fibrosis, but not in those with CHB. In contrast to these findings, Shin *et al*[6] studied a large number of CHB patients and suggested a strong positive linear correlation between fibrosis and APRI. Kim *et al*[16] also concluded that APRI score correlated significantly to fibrosis stage. Güzelbulut *et al*[17] found that the areas under the ROC curves of the APRI score to predict significant fibrosis and cirrhosis were 0.77 and 0.78, respectively. They also mentioned that APRI score is more accurate in the prediction of the absence of both significant fibrosis and cirrhosis with negative predictive values of over 90%. In a recent meta-analysis, Jin *et al*[18] suggested that APRI score showed limited value in predicting CHB related significant fibrosis and cirrhosis and the areas under the ROC curves of APRI score were 0.79 and 0.75, respectively. In our study, we did not find statistically significant relation with APRI score and significant fibrosis. APRI score was significantly higher in cirrhotic patients and the accuracy of APRI score to determine patients with cirrhosis was 72%. In our study, as in that of Güzelbulut *et al*[17], the accuracy of the APRI score in the prediction of the absence of cirrhosis was high with negative predictive values of over 90%. Our study results also showed a statistical association between age and cirrhosis (P = 0.022).

Table 2 Between group comparisons and logistic regression results in chronic hepatitis B patients according to fibrosis stage

Variable	Between group comparisons			Logistic regression analysis	
	No/mild fibrosis (n = 34)	Significant fibrosis (n = 55)	P value	Univariate OR (95%CI)	Multivariate OR (95%CI)
Gender (female/male)	16 (47.1)/18 (52.9)	23 (41.8) /32 (58.2)	0.792	1.2 (0.5-2.9)	-
Age (yr)	40.2 ± 11.7	42.2 ± 13.7	0.473	1.01 (0.9-1.05)	-
HGB	14.4 ± 2.08	14.6 ± 1.8	0.735	1.04 (0.8-1.3)	-
Platelet count (10^3 μL)	203 (176-232)	171 (115-227)	0.010	0.9 (0.9-1)	0.9 (0.9-1)
INR	1.07 ± 0.1	1.13 ± 0.1	0.045	34.5 (1.01-1183.1)	-
Albumine	4.06 ± 0.3	4.01 ± 0.3	0.466	0.6 (0.1-2.3)	-
Total bilirubin (mg/dL)	0.7 (0.5-0.9)	0.8 (0.6-1.1)	0.110	3.05 (0.8-10.8)	-
AST (IU/L)	41.5 (27-73)	47 (32-68)	0.447	1 (0.9-1.01)	-
ALT (IU/L)	57 (33-132)	54 (36-106)	0.866	1 (0.9-1.01)	-
AP (IU/L)	71.5 (62-89)	73 (61-100)	0.630	1.01 (0.9-1.02)	-
GGT (IU/L)	27 (19-48)	36 (23-52)	0.119	1.01 (0.9-1.03)	-
HBV DNA	346 (1.9-1000)	75.7 (1.8-1000)	0.838	1 (0.9-1.01)	-
HBeAg (negative/positive)	30 (88.2)/4 (11.8)	45 (81.8)/10 (18.2)	0.611	1.6 (0.4-5.8)	-
Neutrophil count	3.2 (2.7-4.8)	3.5 (3.04-4.7)	0.569	0.9 (0.6-1.2)	-
Lymphocyte count	1.9 (1.4-2.3)	2 (1.6-2.4)	0.630	0.9 (0.5-1.7)	-
N/L	1.9 (1.3-2.5)	1.8 (1.5-2.2)	0.859	0.8 (0.5-1.3)	-
APRI score	0.5 (0.3-0.9)	0.7 (0.3-1.4)	0.060	1.2 (0.7-2.1)	-

Values are expressed as n (%), mean ± SD or median(25^{th}-75^{th} percentiles). HGB: Hemoglobin; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; AP: Alkaline phosphatase; GGT: Gamma glutamyl transferase; HBV: Hepatitis B virus; HBeAg: Hepatitis B e antigen; N/L: Neutrophil-lymphocyte ratio; APRI: Aspartate aminotransferase/platelet ratio index.

Table 3 Between group comparisons and logistic regression results in chronic hepatitis B patients according to cirrhosis

Variable	Between group comparisons			Logistic regression analysis	
	Non-cirrhotic (n = 76)	Cirrhotic (n = 13)	P value	Univariate OR (95%CI)	Multivariate OR (95%CI)
Gender (female/male)	33 (43.4)/43 (56.6)	6 (46.2)/7 (53.8)	0.999	1.1 (0.3-3.6)	-
Age (yr)	40.2 ± 12.3	49.08 ± 15.04	0.022	1.06 (1.01-1.1)	1.06 (1-1.11)
HGB	14.5 ± 2.03	14.6 ± 1.37	0.891	1.0 (0.7-1.39)	-
Platelet Count (103 μL)	190.5 (152-233.5)	152 (117-175)	0.051	0.9 (0.9-1)	-
INR	1.1 ± 0.1	1.1 ± 0.09	0.250	6.3 (0.09-478.1)	-
Albumine	4.04 ± 0.3	3.9 ± 0.4	0.210	0.2 (0.04-2.01)	-
Total Bilirubin (mg/dL)	0.8 (0.6-1)	1 (0.6-1.3)	0.389	2.09 (0.5-8.7)	-
AST (IU/L)	41.5 (28-65)	66 (40-79)	0.078	1 (0.9-1.01)	-
ALT (IU/L)	54 (33-124)	69 (51-97)	0.419	1 (0.9-1.01)	-
AP (IU/L)	72 (61-89.5)	82 (62-116)	0.225	1.02 (1-1.03)	1.02 (1-1.04)
GGT (IU/L)	28 (20-50.5)	47 (26-50)	0.189	1.01 (1-1.02)	-
HBV DNA	269.5 (2-1000)	10.1 (0.4-1000)	0.339	1 (0.9-1.01)	-
HbeAg (negative/positive)	65 (85.5)/11 (14.5)	10 (76.9)/3 (23.1)	0.423	1.7 (0.4-7.4)	-
Neutrophil count	3.4 (2.8-4.7)	3.8 (3.04-4.1)	0.468	1.05 (0.7-1.5)	-
Lymphocyte count	2 (1.6-2.4)	2 (1.5-2.2)	0.493	0.6 (0.2-1.5)	-
N/L	1.8 (1.3-2.2)	2.04 (1.6-2.8)	0.160	1.3 (0.8-2.07)	-
APRI score	0.5 (0.3-1.08)	1.1 (0.7-1.7)	0.047	1.2 (0.8-2.05)	-

Values are expressed as n (%), mean ± SD or median(25^{th}-75^{th} percentiles). HGB: Hemoglobin; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; AP: Alkaline phosphatase; GGT: Gamma glutamyl transferase; HBV: Hepatitis B virus; HBeAg: Hepatitis B e antigen; N/L: Neutrophil-lymphocyte ratio; APRI: Aspartate aminotransferase/platelet ratio index.

This is an expecting result because the liver damage increases gradually in proportion to the exposure to HBV infection. Patients with CHB above 40 years can be at increased risk of mortality because of liver disease. This can be explained by the increased cirrhosis rates with older age as a host risk factor[19].

With recent evidence, the APRI score, which is used to predict significant fibrosis and cirrhosis in CHC, did not seem as effective in determining fibrosis and cirrhosis in patients with CHB. This can be attributed to differences in the histopathological findings and course of disease. Regenerative nodules are wider in CHB than in CHC[16]. Piecemeal necrosis is more localized and less severe in CHC than in CHB[16]. Hepatic steatosis is an important factor in CHC histology[20]. Disease progression shows a fluctuating course with acute attacks in CHB patients while the progression of fibrosis in CHC is more quiet[16]. For all these reasons, non-invasive markers shown to be effective in CHC should be validated in CHB before use.

The prognosis of patients, who are infected with HBV, depends on the patient's immune response[21]. The hepatitis B virus can be eliminated with a moderate immune response, whereas an excessive response may result in liver damage. HBV persists in the body due to the low-grade immune response. N/L ratio, which is a cheap and easily accessible marker, shows the body's immune response[9].

Table 4 Statistical diagnostic measures and Kappa test results of neutrophil-lymphocyte and aspartate aminotransferase/platelet ratio score in the detection of significant fibrosis and cirrhosis

Variable	Diagnostic measures					Kappa test	
	SEN (95%CI)	SPE (95%CI)	PPR (95%CI)	NPR (95%CI)	AR (95%CI)	κ	*P* value
Significant fibrosis							
N/L (≤ 2.18)	0.73 (0.59-0.84)	0.41 (0.25-0.59)	0.67 (0.53-0.78)	0.48 (0.29-0.67)	0.61 (0.50-0.71)	0.143	0.174
APRI (> 0.56)	0.65 (0.51-0.78)	0.56 (0.38-0.73)	0.71 (0.56-0.83)	0.50 (0.33-0.67)	0.62 (0.51-0.72)	0.209	0.048
Cirrhosis							
N/L (> 2.58)	0.38 (0.14-0.68)	0.87 (0.77-0.64)	0.33 (0.12-0.62)	0.89 (0.80-0.95)	0.80 (0.70-0.88)	0.238	0.024
APRI (> 1.01)	0.62 (0.36-0.86)	0.74 (0.62-0.83)	0.29 (0.13-0.49)	0.92 (0.82-0.97)	0.72 (0.61-0.81)	0.238	0.011

SEN: Sensitivity; SPE: Specifity; PPR: Positive predictive rate; NPR: Negative predictive rate; AR: Accuracy rate; APRI: Aspartate aminotransferase/platelet ratio index; N/L: Neutrophil-lymphocyte ratio.

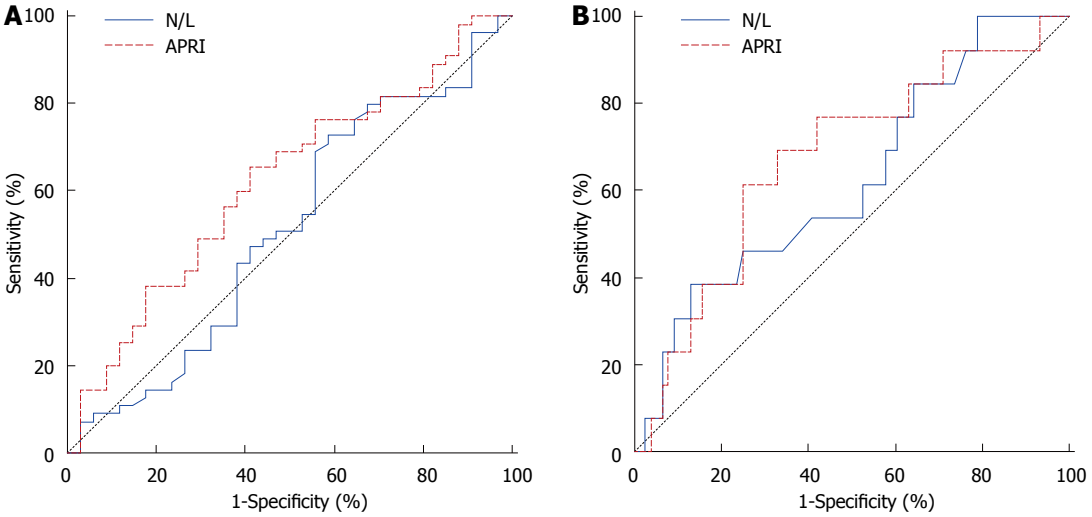

Figure 1 Comparison of receiver operating characteristic curves of neutrophil-lymphocyte ratio and aspartate aminotransferase/platelet ratio index values in identifying significant fibrosis (A) and cirrhosis (B). For significant fibrosis area under receiver operating characteristic (ROC) curves were 0.51 (0.40-0.62) and 0.62 (0.51-0.72) respectively and the differences between two areas were not statistically significant. For cirrhosis, area under ROC curves were 0.62 (0.51-0.72) and 0.67 (0.57-0.77) respectively and the differences between two areas were not statistically significant. N/L: Neutrophil-lymphocyte ratio; APRI: Aspartate aminotransferase/platelet ratio index.

This ratio provides information about two important immune pathways like neutrophils responsible for ongoing inflammation and lymphocytes which have a regulatory role in immune response. Lymphocytes have an impact on liver fibrosis in CHB[22,23]. Alkhouri *et al*[9] showed a relation between N/L ratio and advanced fibrosis in patients with non-alcoholic steatohepatitis. Consequently, N/L ratio may be considered as an important non-invasive marker of liver damage in response to HBV infection.

To our knowledge, our study is the first to evaluate the N/L ratio in CHB disease. In our study, we found a negative and significant relationship between HAI with N/L ratio. This negative relationship demonstrates the important role of lymphocytes in liver damage in CHB. According to our findings fibrosis stage and cirrhosis were not associated with N/L ratio.

All the spectra of biopsies of patients with CHB give rise to the study of the relationship between histological findings with the APRI score and the N/L ratio. The case-control nature of the present study and the number of cases were the limitations of this study.

As with other non-invasive markers APRI and N/L ratio are readily available and inexpensive tests. However, APRI and N/L ratio were not adequate tests to determine either significant fibrosis or cirrhosis in CHB according to our study. For the first time in the literature, this study showed that N/L ratio was negatively correlated with HAI. APRI score may be useful to exclude cirrhosis in CHB patients. Comprehensive and prospective studies are needed to determine the diagnostic value of non-invasive tests for liver damage in CHB.

COMMENTS

Background

Liver biopsy is the standard method to assess liver histology in chronic hepatitis B (CHB) disease. Due to the limitations of liver biopsy, the use of non-invasive markers has emerged in recent years. The aspartate aminotransferase/platelet ratio index (APRI) is used to determine chronic hepatitis C (CHC) patients with advanced fibrosis. Neutrophil-lymphocyte (N/L) ratio is higher in patients with advanced fibrosis and considered as a novel non-invasive marker to predict advanced disease in non-alcoholic steatohepatitis. But up to now, no study evaluated the efficacy of N/L ratio to predict liver damage in CHB.

Research frontiers

The APRI has been used to determine CHC patients with advanced fibrosis. APRI also predicts significant fibrosis in CHB. The N/L ratio can be calculated

easily from complete blood counts and is an easily accessible marker which indicates the state of inflammation in the body. The N/L ratio is higher in patients with non-alcoholic steatohepatitis (NASH) and advanced fibrosis. Also the N/L ratio may be used as a novel non-invasive marker to predict advanced disease in NASH. The research hotspot is to evaluate the N/L ratio to determine hepatic damage and fibrosis in patients with CHB and compare its effectiveness with APRI.

Innovations and breakthroughs

In the present study, the APRI score was significantly higher in CHB patients with cirrhosis. The APRI score was higher in significant fibrosis but it was not statistically significant. While the N/L ratio was not related with significant fibrosis and cirrhosis, it was found to be negatively correlated with HAI in patients with CHB.

Applications

The study results suggest that the N/L ratio is negatively correlated with HAI. APRI score may be useful to exclude cirrhosis in CHB patients.

Terminology

The APRI score was calculated with the formula (AST/40)/platelet (10^9/L) × 100. The N/L ratio was calculated using the values of neutrophils and lymphocytes obtained from the patients complete blood counts.

Peer review

The authors provide an interesting and potentially important manuscript describing noninvasive assessment of liver Fibrosis in CHB. The authors showed that the platelet count is a unique independent predictive factor for liver fibrosis in CHB.

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