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AST-platelet ratio index in the prediction of significant fibrosis and cirrhosis in patients with chronic hepatitis B

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Background/aims: *We aimed to evaluate the diagnostic accuracy of AST-platelet ratio index in the prediction of significant fibrosis and cirrhosis in chronic hepatitis B patients by comparison with liver biopsy.* ***Materials and Methods:*** *We retrospectively reviewed our computerized data of chronic hepatitis B patients who attended the Gastroenterology Clinic from 2004-2009. Treatment-naive chronic hepatitis B patients who had undergone liver biopsy were included in this study. The degree of fibrosis was scored according to the Ishak staging system. Significant fibrosis was defined as F3-6 and cirrhosis as F5-6. AST-platelet ratio index was calculated based on the original studies. Tests results were compared between the groups F0-2 versus F3-6 and F0-4 versus F5-6.* ***Results:*** *Two hundred and fifty consecutive patients with chronic hepatitis B were included in this study. The area under the ROC curves of AST-platelet ratio index to predict significant fibrosis and cirrhosis were 0.779 and 0.781, respectively. Using cut-off values ≤0.5 and >1.5, significant fibrosis was excluded with a negative predictive value of 91.30% and sensitivity of 87.69% and predicted with a positive predictive value of 59.52% and specificity of 90.81% in 53.60% of patients. Using cut-off values ≤1 and >2, cirrhosis was excluded with a negative predictive value of 92.09% and sensitivity of 64.10% and predicted with a positive predictive value of 33.33% and specificity of 91.47% in 81.60% of patients.* ***Conclusions:*** *AST-platelet ratio index may be a useful noninvasive marker in the exclusion of both significant fibrosis and cirrhosis in patients with chronic hepatitis B. However, it is not accurate in the prediction of either significant fibrosis or cirrhosis.*

Key words: AST-platelet ratio index, chronic hepatitis B, fibrosis

Kronik hepatit B'li hastalarda belirgin fibrozis ve sirozun belirlenmesinde AST-Platelet oranı indeksinin yeri

Amaç: *Kronik hepatit B'li hastalarda belirgin fibrozis ve sirozun belirlenmesinde AST-platelet oranı indeksinin tanısal güvenilirliğini karaciğer biyopsisi ile karşılaştırmalı olarak değerlendirmek.* ***Yöntem ve Gereç:*** *2004-2009 yıllarında Gastroenteroloji Kliniği'ne kronik hepatit B tanısı ile başvuran hastaların bilgisayar kayıtlarını retrospektif olarak inceledik. Karaciğer biyopsisi yapılmış olan hiç tedavi olmamış kronik hepatit B'li hastalar çalışmaya alındı. Fibrozisin derecesi Ishak sistemine göre belirlendi. F3-6 belirgin fibrozis ve F5-6 siroz olarak kabul edildi. AST-platelet oranı indeksi orijinal çalışmalar esas alınarak hesaplandı. Test sonuçları F0-2 ile F3-6 olan gruplar ve F0-4 ile F5-6 olan gruplar arasında karşılaştırıldı.* ***Bulgular:*** *250 kronik hepatit B'li hasta çalışmaya alındı. Belirgin fibrozis ve sirozun belirlenmesinde AST-platelet oranı indeksi için ROC eğrisi altında kalan alan sırası ile 0.779 ve 0.781 idi. ≤0.5 ve >1.5 sınır değerleri kullanıldığında hastaların %53.60'ında belirgin fibrozis %91.30 negatif prediktif değer ve %87.69 sensitivite ile dışlandı, %59.52 pozitif prediktif değer ve %90.81 spesifite ile doğrulandı. ≤1 ve >2 sınır değerleri kullanıldığında hastaların %81.60'ında siroz %92.09 negatif prediktif değer ve %64.10 sensitivite ile dışlandı, %33.33% pozitif prediktif değer ve %91.47 spesifite doğrulandı.* ***Sonuç:*** *Kronik hepatit B'li hastalarda AST-platelet oranı indeksi hem belirgin fibrozis hem de sirozun dışlanmasında güvenilir bir noninvaziv belirteçtir. Ancak belirgin fibrozis ve sirozun doğrulanmasında yeterince güvenilir değildir.*

Anahtar kelimeler: AST-platelet oranı indeksi, kronik hepatit B, fibrozis

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INTRODUCTION

Chronic hepatitis B virus (HBV) infection is a major public health problem. It is estimated that 350 million of the world's population are chronically infected with HBV (1,2). The spectrum of disease ranges from inactive carrier state to cirrhosis and hepatocellular carcinoma (HCC) (2). HBV-related end stage liver disease and HCC are also the major causes of liver transplantation (2).

The main goal of therapy is to prevent the progression of fibrosis and the development of end stage liver disease and HCC, which can be achieved via suppression of HBV DNA replication in a sustained manner and HBeAg seroconversion if it is positive. Deciding on antiviral therapy for chronic HBV infection depends on the degree of hepatic inflammation and/or fibrosis along with HBV DNA levels and serum alanine aminotransferase (ALT) levels (1,2).

Although liver biopsy remains the gold standard method for the assessment of hepatic fibrosis, it cannot be performed repeatedly due to its invasiveness, cost and risk of serious complications (3-7). Under- or overestimation of the degree of hepatic fibrosis with inter- and intraobserver discrepancies of 10%-20% and sampling errors are other limitations (4,7,8).

Therefore, there is need for noninvasive tests to assess hepatic fibrosis. Several noninvasive tests have been developed to predict the presence of significant fibrosis and cirrhosis in patients with chronic hepatitis C (CHC) (9-13). Of these tests, aspartate aminotransferase (AST)/platelet ratio index (APRI) was proposed by Wai et al. (9) to predict significant fibrosis and cirrhosis in CHC patients. The main advantage of APRI over other noninvasive tests is that it is based on readily available blood tests and simple to use. Although there are many studies evaluating APRI in CHC patients, our knowledge about its usefulness in chronic hepatitis B (CHB) patients is limited. Because the course of CHB is different from that of CHC, results of studies evaluating APRI in CHC may not be applied to CHB patients directly (14-16).

In the present study, we aimed to evaluate the diagnostic accuracy of APRI in the prediction of significant fibrosis and cirrhosis in chronic HBV monoinfected patients by comparison with liver biopsy.

MATERIALS AND METHODS

We retrospectively reviewed our computerized data of HBV monoinfected patients who attended the Gastroenterology Clinic from 2004-2009. Two hundred and fifty consecutive HBV monoinfected patients with the following criteria were included in this study: 1) HBsAg positivity for more than six months, 2) HBV DNA ≥2,000 IU/ml, 3) liver biopsy prior to treatment, 4) laboratory test results allowing the calculation of APRI obtained within three months from the date of liver biopsy, 5) absence of human immunodeficiency virus (HIV) and/or HCV and/or HDV coinfection, 6) absence of other liver diseases, 7) absence of HCC, 8) absence of prior liver transplantation, and 9) abstinence from alcohol abuse for more than six months.

All liver biopsy specimens were analyzed by a single pathologist. The degree of fibrosis was scored according to the Ishak system, and no-mild fibrosis was defined as F0-2, significant fibrosis as F3-6, and cirrhosis as F5-6.

Laboratory test results, including AST, ALT, gamma-glutamyl transferase (GGT), and platelet count were collected. APRI was calculated based on the following formula: APRI=(AST/ULN)/platelet x 100.

We compared the diagnostic accuracy of APRI between the groups F0-2 (no-mild fibrosis) vs F3-6 (significant fibrosis) and F0-4 (no cirrhosis) vs F5-6 (cirrhosis).

Statistical analysis was made using NCSS (Number Cruncher Statistical System) 2007 and PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA). Quantitative variables were presented as means (±SD), standard deviation, median, counts and percentages. During the evaluation of the study data, along with the descriptive statistical methods, parameters with normal distribution for the comparison of qualitative data were evaluated using one-way ANOVA and Tukey HSD test and Student's t-test, and cases who did not have a normal distribution were evaluated using Kruskal-Wallis analysis and Mann-Whitney U test. The qualitative data were evaluated using chi-square test. Results were given in 95% confidence interval and significance was accepted at the $p<0.05$ level. The present study was approved by the local ethics committee.

RESULTS

Two hundred and fifty patients with CHB were included in this study. All patients were white and 57.6% were male (n=144), with a mean age of 38.67±14.73 years. Sixty-five (26%) patients had

significant fibrosis (F3-6) and 39 (15.6%) had cirrhosis (F5-6). The main characteristics of patients are shown in Table 1.

AST, AST/ULN and APRI were significantly higher and platelet count was significantly lower in patients with significant fibrosis than in those without significant fibrosis (all p=0.001). AST and APRI were significantly higher and platelet count was significantly lower in patients with cirrhosis than in those without cirrhosis (p=0.019, p=0.001, p=0.001, respectively). AST/ULN was higher in patients with cirrhosis than in those without cirrhosis, but the difference was not significant (p=0.065). ALT and ALT/ULN were not different between patients with and without significant fibrosis, or between those with and without cirrhosis. Mean age, platelet count, AST, AST/ULN, ALT, ALT/ULN, and APRI in patients with no-mild fibrosis (F0-2) vs significant fibrosis (F3-6) and with no cirrhosis (F0-4) vs cirrhosis (F5-6) are shown in Table 2.

Table 1. Main characteristics of patients

	Mean±SD (median)
Age (Mean SD)	38.67±14.73
Sex (Male) (%)	144 (57.6)
Platelet (x1000)	211.79±78.45
AST (IU/mL)	59.01±57.11
ALT (IU/mL)	92.83±109.54
AST (xULN)	1.81±1.79
ALT (xULN)	2.27±2.66
Fibrosis	n (%)
F0	99 (39.6)
F1	42 (16.8)
F2	44 (17.6)
F3	20 (8)
F4	6 (2.4)
F5	9 (3.6)
F6	30 (12)

Receiver operating characteristic (ROC) curves of the APRI in the prediction of significant fibrosis and cirrhosis are plotted in Figures 1 and 2. The area under the ROC curves (AUROC) of APRI to predict significant fibrosis (F3-6) and cirrhosis (F5-6) were 0.779 and 0.781, respectively (Table 3).

For patients with an APRI of ≤0.5, 84 of 92 did not have significant fibrosis, and for those with an APRI of >1.5, 25 of 42 had significant fibrosis. An APRI ≤0.5 excluded significant fibrosis in 91.30% (negative predictive value, NPV) of patients, with a sensitivity of 87.69%, while an APRI >1.5 predicted significant fibrosis in 59.52% (positive predictive value, PPV) of patients, with a specificity of 90.81%, in 53.60% of patients (Table 4).

For patients with an APRI of ≤1, 163 of 177 did not have cirrhosis, and for those with an APRI of >2, 9 of 27 had cirrhosis. An APRI ≤1 excluded cirrhosis in 92.09% (NPV) of patients, with a sensitivity of 64.10%, and an APRI >2 predicted cirrhosis in 33.33% (PPV) of patients, with a specificity of 91.47%, in 81.60% of patients (Table 5).

Diagnostic accuracy of the APRI in the prediction of significant fibrosis and cirrhosis are shown in Tables 4 and 5.

DISCUSSION

APRI was first proposed by Wai et al. (9) to predict significant fibrosis and cirrhosis in CHC patients and avoided the need for liver biopsy in a substantial proportion of patients. Subsequently, many studies were performed to evaluate the diagnostic accuracy of APRI to predict significant fibrosis and cirrhosis in CHC patients. The AUROC of the test ranged between 0.69-0.92 to predict significant fibrosis and between 0.765-0.92 to predict advan-

Table 2. Comparison of variables associated with the presence of significant fibrosis and cirrhosis

	Fibrosis			Fibrosis		
	F 0-2 (n=185) Mean±SD (median)	F 3-6 (n=65) Mean±SD (median)	*p*	F 0-4 (n=211) Mean±SD (median)	F 5-6 (n=39) Mean±SD (median)	*p*
Age++	36.03±13.70	46.20±15.06	0.001**	36.77±13.83	48.82±15.49	0.001**
Platelet++	229.80±75.10	160.55±64.95	0.001**	225.05±74.40	140.09±60.36	0.001**
AST+	52.39±52.15 (39)	77.84±66.21 (55)	0.001**	54.83±51.25 (41)	81.59±78.97 (47)	0.019*
ALT+	95.32±117.04 (62)	85.74±82.61 (57)	0.924	94.84±112.04 (64)	81.95±95.38 (52)	0.253
AST/ULN+	1.62±1.73 (1.19)	2.32±1.91 (1,61)	0.001**	1.69±1.67 (1.26)	2.39±2.29 (1.30)	0.065
ALT/ULN+	2.29±2.71 (1,5)	2.19±2.50 (1.4)	0.987	2.29±2.60 (1.55)	2.13±2.99 (1.27)	0.210
APRI	0.76±0.74 (0.56)	1.67±1.57 (1.14)	0.001**	0.83±0.81 (0.58)	1.91±1.82 (1.25)	0.001**

++Student t test +Mann-Whitney U test *p<0.05 **p<0.01

ced fibrosis or cirrhosis depending on the study populations. APRI avoided the need for liver biopsy in nearly one-third to one-half of the patients using the traditional cut-off values in patients with CHC (7,17-19).

Although many studies were performed to evaluate APRI in CHC patients, our knowledge about its usefulness in CHB patients is limited. It is known that the course of CHB is different from that of CHC. In both CHB and CHC, thrombocytopenia is

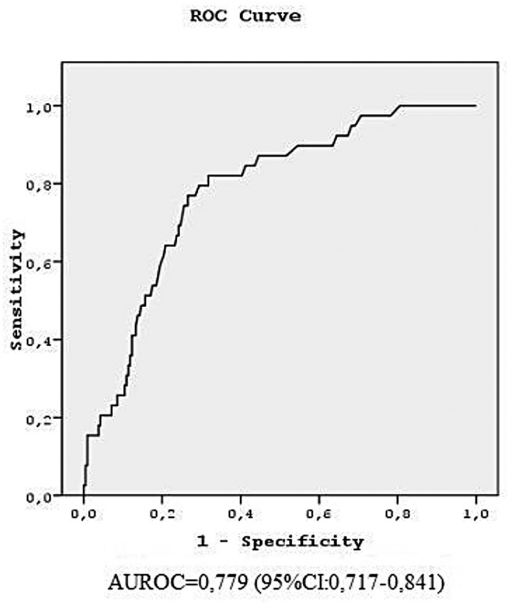

Figure 1. ROC curve of APRI in the prediction of significant fibrosis

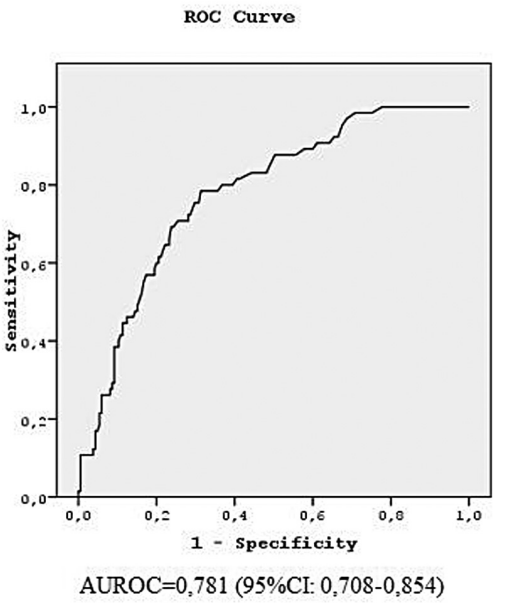

Figure 2. ROC curve of APRI in the prediction of cirrhosis

Table 3. AUROC of APRI in the prediction of significant fibrosis and cirrhosis

	Significant fibrosis (F0-2 vs F3-6)		Cirrhosis (F0-4 vs F5-6)	
Test	Area	95% CI	Area	95% CI
APRI	0.779	0.717-0.841	0.781	0.708-0.854

CI: Confidence interval.

Table 4. Diagnostic accuracy of tests in the prediction of significant fibrosis (F3-6)

		Total	Fibrosis		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
			0-2	3-6				
APRI	≤ 0.5	92	84	8	87.69	45.41	36.07	91.30
	>0.5	158	101	57				
	≤ 1.5	208	168	40	38.46	90.81	59.52	80.77
	>1.5	42	17	25				

NPV: Negative predictive value. PPV: Positive predictive value.

Table 5. Diagnostic accuracy of tests in the prediction of cirrhosis (F5-6)

		Total	Fibrosis		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
			0-4	5-6				
APRI	≤ 1	177	163	14	64.10	77.25	34.25	92.09
	>1	73	48	25				
	≤ 2	223	193	30	23.07	91.47	33.33	86.55
	>2	27	18	9				

NPV: Negative predictive value. PPV: Positive predictive value.

the result of increased sequestration and destruction of platelets due to liver fibrosis and splenomegaly and of decreased production of platelets due to decreased production of thrombopoietin by hepatocytes (14,16). AST elevation is also the result of increased fibrosis due to the decreased clearance of AST and mitochondrial injury in both CHB and CHC (14). While patients with CHB commonly experience acute flares followed by resolution of necroinflammatory activity with fluctuating transaminase levels, in patients with CHC, progression of fibrosis is silent and often without acute flares with stable transaminase levels (8,14,16). There are also differences in liver histology between patients with CHC and CHB. Regenerative nodules are larger in CHB, while they are smaller in CHC (16). In contrast to CHB, steatosis is an important feature of CHC (15,20). Therefore, APRI must be validated in CHB patients before applying the results of studies evaluating APRI in CHC.

In the present study, the AUROCs of APRI to predict significant fibrosis and cirrhosis were 0.779 and 0.781, respectively. As measured by the AUROC, APRI seems to be accurate in the prediction of both significant fibrosis and cirrhosis in CHB patients; however, it is more accurate in the prediction of the absence of both significant fibrosis and cirrhosis with high NPVs. On the other hand, diagnostic value of the test in the prediction of the presence of both significant fibrosis and cirrhosis was limited, with low PPVs.

APRI was evaluated in patients with CHB firstly by Wai et al. (14). The AUROC of APRI to predict significant fibrosis and cirrhosis were 0.63 and 0.64, respectively. They concluded that APRI was not accurate to predict either significant fibrosis or cirrhosis in patients with CHB. Subsequently, several studies were performed to evaluate APRI to predict significant fibrosis and/or cirrhosis in CHB patients and they showed various results. The AUROC of APRI varied between studies as did NPV and PPV.

Similar to Wai et al.'s study, the AUROCs of APRI to predict significant fibrosis and cirrhosis were 0.673 and 0.626, respectively, in Chang et al.'s study (8). In a study by Sebastiani et al. (15), the AUROCs of APRI to predict significant fibrosis and cirrhosis were 0.72 and 0.64, respectively. PPV of APRI in the prediction of significant fibrosis was higher than NPV, and NPV of the test in the prediction of cirrhosis was higher than PPV. Shin et al. (21) evaluated APRI in the prediction of significant fibrosis in patients with CHB as well as CHC and nonalcoholic fatty liver disease. The AUROC of APRI was 0.85 in the prediction of significant fibrosis in CHB patients. In that study, APRI worked better in the prediction of the presence of significant fibrosis than in the exclusion of the presence of significant fibrosis, with a high PPV and a low NPV. In Kim et al.'s (16) study, the AUROC of APRI to predict cirrhosis was 0.75. Similar to our study, APRI was better in the exclusion of the presence of cirrhosis than in the prediction of the presence of cirrhosis. However, the diagnostic value of APRI in the prediction of significant fibrosis was not evaluated in that study. These different results may be related to patient characteristics in various studies. They may be due to the lower prevalence of significant fibrosis and cirrhosis in our study (26% and 15.6%) than in previous studies, which may overestimate NPV (14,16,21).

Alternatively, Zhang et al. (22) evaluated the combination of APRI and hyaluronic acid (HA) to predict significant fibrosis in patients with CHB, and in that study, the PPV and specificity of APRI were low and increased significantly when HA was added.

According to our study, APRI may be useful in the exclusion but not in the prediction of significant fibrosis and cirrhosis in patients with CHB, and the results of studies evaluating APRI in CHC cannot be applied to CHB directly. This may be due to the different clinical course and liver fibrosis progression of CHB from those of CHC as noted above (15,16). In our study, platelet counts were lower in patients with significant fibrosis and cirrhosis than in those without significant fibrosis and cirrhosis. However, in our study, AST/ULN levels were not different between patients with and without cirrhosis, although AST and AST/ULN levels were significantly higher in patients with significant fibrosis than in those without significant fibrosis. Normal or mildly elevated transaminase levels between flares despite the presence of advanced fibrosis might lead to false-negative results. Thus, fluctuations in AST levels might alter the NPV and PPV of APRI (16).

In conclusion, APRI may be a useful noninvasive marker, especially in the exclusion of both significant fibrosis and cirrhosis in patients with CHB. If it is lower than the given cut-off levels, APRI may avoid the need for liver biopsy in a substantial proportion of patients. Results of studies evaluating APRI in CHC cannot be applied to CHB patients directly.

REFERENCES

1. Lok AS, McMahon BJ. Chronic hepatitis B: update 2009. Hepatology 2009; 50: 661-2.
2. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: management of chronic hepatitis B. J Hepatol 2009; 50: 227-42.
3. Kawamoto M, Mizuguchi T, Katsuramaki T, et al. Assessment of liver fibrosis by a noninvasive method of transient elastography and biochemical markers. World J Gastroenterol 2006; 12: 4325-30.
4. Friedrich-Rust M, Ong MF, Herrmann E, et al. Real-time elastography for noninvasive assessment of liver fibrosis in chronic viral hepatitis. AJR Am J Roentgenol 2007; 188: 758-64.
5. Rockey DC, Caldwell SH, Goodman ZD, et al. Liver biopsy. Hepatology 2009; 49: 1017-44.
6. Kim DY, Kim SU, Ahn SH, et al. Usefulness of FibroScan for detection of early compensated liver cirrhosis in chronic hepatitis B. Dig Dis Sci 2009; 54: 1758-63.
7. Silva Jr RG, Fakhouri R, Nascimento TV, et al. Aspartate aminotransferase-to-platelet ratio index for fibrosis and cirrhosis prediction in chronic hepatitis C patients. Braz J Infect Dis 2008; 12: 15-9.
8. Chang PE, Lui HF, Chau YP, et al. Prospective evaluation of transient elastography for the diagnosis of hepatic fibrosis in Asians: comparison with liver biopsy and aspartate transaminase platelet ratio index. Aliment Pharmacol Ther 2008; 28: 51-61.
9. Wai CT, Greenson JK, Fontana RJ, et al. A simple noninvasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C. Hepatology 2003; 38: 518-26.
10. Forns X, Ampurdanes S, Lovet JM, et al. Identification of chronic hepatitis C patients without hepatic fibrosis by a simple predictive model. Hepatology 2002; 36: 986-92.
11. Koda M, Matunaga Y, Kawakami M, et al. Fibroindex, a practical index for predicting significant fibrosis in patients with chronic hepatitis C. Hepatology 2007; 45: 297-306.
12. Vallet-Pichard A, Mallet V, Nalpas B, et al. FIB-4: an inexpensive and accurate marker of fibrosis in HCV infection. Comparison with liver biopsy and Fibrotest. Hepatology 2007; 46: 32-6.
13. Sterling LK, Lissen E, Clumeck N, et al. for the APRICOT Clinical Investigators. Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. Hepatology 2006; 43: 1317-25.
14. Wai CT, Cheng CL, Wee A, et al. Non-invasive models for predicting histology in patients with chronic hepatitis B. Liver Int 2006; 26: 666-72.
15. Sebastiani G, Vario A, Guido M, Alberti A. Sequential algorithms combining non-invasive markers and biopsy for the assessment of liver fibrosis in chronic hepatitis B. World J Gastroenterol 2007; 13: 525-31.
16. Kim BK, Kim SA, Park YN, et al. Noninvasive models to predict liver cirrhosis in patients with chronic hepatitis B. Liver Int 2007; 27: 969-76.
17. Cheung RC, Currie S, Shen H, et al. Can we predict the degree of fibrosis in chronic hepatitis C patients using routine blood tests in our daily practice? J Clin Gastroenterol 2008; 42: 827-34.
18. Leroy V, Hilleret MN, Sturm N, et al. Prospective comparison of six non-invasive scores for the diagnosis of liver fibrosis in chronic hepatitis C. J Hepatol 2007; 46: 775-82.
19. Halfon P, Bacq Y, De Murret A, et al. Comparison of test performance profile for blood tests of liver fibrosis in chronic hepatitis C. J Hepatol 2007; 46: 395-402.
20. Altıparmak E, Koklu S, Yalinkilic M, et al. Viral and host causes of fatty liver in chronic hepatitis B. World J Gastroenterol 2005; 11: 3056-9.
21. Shin WG, Park SH, Jun SY, et al. Simple tests to predict hepatic fibrosis in nonalcoholic chronic liver diseases. Gut Liver 2007; 1: 145-50.
22. Zhang YX, Wu WJ, Zhang YZ, et al. Noninvasive assessment of liver fibrosis with combined serum aminotransferase/platelet ratio index and hyaluronic acid in patients with chronic hepatitis B. World J Gastroenterol 2008; 14: 7117-21.