Original research

Albumin- Bilirubin Score as a Non-Invasive Serum Biomarker for Advanced Liver Fibrosis and Cirrhosis in Egyptian Patients with Chronic Hepatitis C Infection: A Case-Control Study

Dina M. Ali [1], Mohamed A. AlMoslemany [2], Osama Mohamed [2], Khaled Raafat[3]

[1]Tropical Medicine Department, Faculty of Human Medicine, Zagazig University, Egypt.

[2] Intern Physicians, Menoufia University Hospitals, Egypt.

[3] Internal Medicine Department, Faculty of Human Medicine, Ain Shams University, Egypt.

Correspondence to: Dina M. Ali, Tropical Medicine Department, Faculty of Human Medicine, Zagazig University, Egypt. E-mail: dalali@zu.edu.eg, Tel: (+20) 01228125569, Fax (+2055-2307830), Postal Code: 44519.

DOI: 10.21608/ajgh.2022.173503.1019.

Type of manuscript: original research.

Date of submission: 08- November-2022.

Revised: 25- December-2022.

Accepted: 28- December-2022.

First online: 1-January-2023.

Original research

Abstract

Background: In many health systems, primary care is the main source of health care services. Liver cirrhosis is a silent disease that causes no signs or symptoms until decompensation occurs. Therefore, a simple and readily accessible tool for predicting advanced liver fibrosis and cirrhosis is needed to aid general practitioners in primary care settings. **Aim:** To explore the predictive performance of Albumin Bilirubin (ALBI) score as a non-invasive serum biomarker for advanced liver fibrosis and cirrhosis. **Methods:** This case-control study was conducted at Zagazig University Hospitals, Egypt, and comprised 400 participants divided into two equal groups. Group (I): 200 chronic HCV patients with advanced liver fibrosis and cirrhosis [F3-F4] and Group (II): 200 healthy controls. ALBI score was calculated for all study participants. **Results:** The AUROC for the ALBI score was 0.832 (95% CI: 0.787-0.872) (p-value <0.001), sensitivity= 74.8%, specificity= 80.2%, PPV= 86.8%, NPV =64.6%, and positive likelihood ratio=3.77. The cut-off value to differentiate chronic HCV patients with advanced liver fibrosis and cirrhosis from healthy controls was -2.781. Sub-group analysis of chronic HCV cases showed a statistically significant difference in the mean ALBI score between (F3) and (F4) cases (p-value<0.0001) with an AUROC of 0.654 (p-value=0.028). **Conclusion:** ALBI score is reliable for predicting advanced liver fibrosis and cirrhosis and could be valuable in primary care.

Keywords: ALBI score, liver fibrosis, liver cirrhosis, non-invasive markers, hepatitis C, primary care, Egypt.

Introduction

In some countries, the mortality rates for liver diseases are four times higher than in the 1970s [1]. The progression of liver fibrosis, which has no signs or symptoms, leads to liver cirrhosis, decompensation, hepatocellular carcinoma (HCC), and eventually death [2]. Liver fibrosis develops due to chronic exposure to various causes of liver injury. Unfortunately, most individuals are unaware that they have liver cirrhosis until a decompensating event occurs [3].

Original research

The liver biopsy is the gold standard for identifying and quantifying liver fibrosis. However, the invasive nature of the procedure, related hazards, and sample errors have resulted in low patient acceptability. Consequently, there is considerable interest in establishing the diagnosis of hepatic fibrosis without the use of liver biopsy, which necessitates the development of non-invasive liver fibrosis markers [4]. Several non-invasive blood biomarker tests, such as Fibrosis-4 (FIB-4), Aspartate Transaminase to Platelets Ratio Index (APRI), and Fibro-test, are already available, in addition to advanced imaging techniques, including Transient Elastography (TE) and Magnetic Resonance Imaging (MRI) [5-7].

The UK Lancet Liver Commission's main recommendation was to "strengthen early diagnosis and treatment of liver disease in primary care." A risk assessment tool that relies on regular blood results (typically already accessible) could thus be clinically beneficial [1].

The Albumin-Bilirubin (ALBI) score was initially developed to predict the prognosis in cirrhotic patients with or without HCC. It includes only two parameters, serum albumin, and bilirubin, both of which are objective indicators. According to this score, patients are classified as grade 1 with lowest mortality risk (ALBI score $\leq$ -2.60), ALBI grade 2 (score -2.60 < and $\leq$ - 1.39) with intermediate mortality risk, and grade 3 (score >-1.39) with highest mortality risk [8].

The ability of the ALBI score to predict advanced liver fibrosis and cirrhosis has not been thoroughly investigated. Therefore, we conducted this study to explore the performance of the ALBI score as a predictor of advanced liver fibrosis and cirrhosis (F3 and F4) in chronic Hepatitis C (HCV) Egyptian patients compared to healthy individuals.

Methods

a) Study setting and sample size

This case-control study was conducted at Zagazig University Hospitals, Egypt, between 2018-2020. The study included a total of 400 participants. The sample size was

Original research

calculated from the results of a previous study [8] using MedCalc software according to the following parameters: type I error (α) =0.05 and type II error (β) = 0.20.

b) Study population

The study comprised two equal groups: Group (I): 200 Egyptian patients with chronic HCV infection who were seeking Direct Acting Antiviral (DAAs) treatment for chronic HCV infection, and Group (II): included 200 healthy controls. The patients were eligible for enrollment in the study if they met the following inclusion criteria: **(1)** age≥18 years, **(2)** male or female, **(3)** Chronic HCV infection confirmed by the presence of positive serum HCV antibodies and by quantitative Polymerase Chain Reaction (PCR), **(4)** advanced liver fibrosis and cirrhosis (F3&F4) diagnosed by fibroscan, **(5)** no evidence of HCC by both pelvi-abdominal ultrasound and serum Alfa-fetoprotein (AFP) level. The patients were excluded from the study if they met the following exclusion criteria: **(1)** age<18 years, **(2)** evidence of decompensated liver disease, **(3)** evidence of HCC by pelvi-abdominal ultrasound, triphasic pelvi-abdominal Computed Tomography (CT), and serum AFP level, **(4)** other causes of liver fibrosis and cirrhosis. TE was performed for all chronic HCV-infected patients using Echosense 502 machine. The results of TE were interpreted as follows: F0-F1= 2-7 kPa, F2=8-9 kPa, F3= 9.5-13 kPa, F4= 14 kPa or higher [9]. All healthy controls tested negative for serum HCV antibodies and HBs Ag. The pelvi-abdominal ultrasound was performed for the control group and was unremarkable.

c) Calculation of ALBI score

The ALBI score was calculated according to its original report [10]:

$$\textbf{ALBI score} = \textbf{Log}_{10}\ \textbf{T-Bil (µmol/L)} \times \textbf{0.66} + \textbf{Alb (g/L)} \times (-\textbf{0.085}).$$

d) Ethical considerations

The study followed the Declaration of Helsinki's ethical guidelines for medical research and was approved by the Institutional Review Board of the Faculty of Human Medicine

Original research

at Zagazig University (ZU-IRB No.9625). All participants signed a written informed consent form.

Statistical analysis

The Statistical Package for Service Solution (IBM SPSS version 26) was used to generate the results. The normality of the data was tested using Kolmogorov-Smirnov single sample test. Numerical variables were summarized as mean and standard deviation. Qualitative variables were expressed as frequencies and percentages. Comparison between numerical variables was made using two independent samples T-test. A comparison between qualitative variables was created using the Chi-Square test. The optimal cut-off value was calculated using the Receiver Operator Characteristic Curve (ROC) analysis. Probability is considered significant if equal to or less than 0.05.

Results

a) Characteristics of the study participants

The study included 200 chronic HCV patients with advanced liver fibrosis and established cirrhosis (F3&F4). Of them, (n=88, 44%) were males and (n=112, 56%) were females. At the same time, the control group included 200 healthy individuals (n=96, 48%) were males and (n= 104, 52%) were females; (p value=0.4). The mean ±SD age for chronic HCV cases was 58.8±6.7 compared to 57.21±4.2 for the healthy controls (p value=0.15). Demographic and laboratory characteristics of both groups are shown in **Table (1)**. Both groups had a statistically significant difference regarding serum bilirubin, albumin, ALT, AST, WBCs, and platelets count (p-value <0.0001). Based on the fibroscan results (n=160, 80%) patients had F4 and (n= 40, 20%) had F3 liver fibrosis. The mean fibroscan result for the chronic HCV cases was 26.5±14.4 kPa (range: 11-75).

Original research

Table 1. Demographic and laboratory characteristics of the study participants.

Variable (Mean ±SD)	Cases (n= 200)	Controls (n=200)	P- value
Age (years)	58.8±6.7	57.21±4.2	0.15
Sex (n, %)			
Females	112 (56%)	104 (52%)	0.4
Males	88 (44%)	96 (48%)	
Bilirubin (mg/dl)	1.05±0.65	0.63±0.38	**<0.0001**
Albumin(g/L)	3.66±0.65	4.26±0.40	**<0.0001**
ALT (IU/L)	64.8±35.9	39±31.6	**<0.0001**
AST (IU/L)	75.1±52.8	51.5±57.3	**<0.0001**
FBC			
• WBCs ($\times 10^9$/L)	5.53±2.1	7.4±1.9	**<0.0001**
• HB (g/dl)	13.49±4.1	14±1.5	0.09
• Platelets ($\times 10^9$/L)	127.8±63.6	204.1±72.67	**<0.0001**

b) Comparison of ALBI score in both chronic HCV cases and healthy controls

There was a highly statistically significant difference between cases and controls as regards both ALBI grades and score, as shown in **Table (2)**. According to ALBI grades, (n=70, 35%) of chronic HCV patients had values corresponding to ALBI grade 1, (n=120, 60%) patients had values fitting ALBI grade 2, and (n=10, 5%) patients had a score corresponding to ALBI grade 3. Regarding the controls, (n=177, 88.5%) had values corresponding to ALBI grade 1, (n=22, 11%), and (n=1, 0.5%) had values corresponding to ALBI grade 2 and 3, respectively (p-value <0.0001). The mean ±SD ALBI score for the chronic HCV cases was -2.32±0.62 and -2.96±0.40 for the controls, respectively (p-value <0.0001).

Original research

Table 2. Comparison of ALBI score in chronic HCV cases and healthy controls.

Variable	Cases (n=200)	Controls (n=200)	P-Value
ALBI Grade (n,%)			
Grade 1	70 (35%)	177 (88.5%)	**<0.0001**
Grade 2	120 (60%)	22 (11%)	
Grade 3	10 (5%)	1 (0.5%)	
ALBI Score			
Mean ±SD	-2.32±0.62	-2.96±0.40	**<0.0001**
Range	(-4.06- 0.39)	(-3.78- -1.19)	

c) Performance of ALBI score as a non-invasive serum biomarker of advanced liver fibrosis and cirrhosis

The performance of the ALBI score is summarized in **Table (3)**, where the sensitivity was = 74.8% (95% CI: 68.2-80.6%), specificity= 80.2% (95% CI: 71.7-87%), PPV= 86.8% (95% CI: 81.9-90.5%), NPV =64.6% (95% CI: 58.6-70.2%), and positive likelihood ratio (+LR) =3.77 (95% CI: 2.59-5.48). The AUROC was 0.832 (95% CI: 0.787-0.872), (p-value < 0.001) as shown in **Figure (1)**. The cutoff value to differentiate chronic HCV patients with advanced liver fibrosis and cirrhosis from healthy controls was -2.781.

Table 3. Performance of ALBI score as a non-invasive index of advanced liver fibrosis and cirrhosis.

Indicator	Result (95% CI)
Cut-off point	-2.781
AUROC	0.832 (0.787-0.872)
Sensitivity	74.8% (68.2-80.6%)
Specificity	80.2% (71.7-87%)
Positive Predictive Value (PPV)	86.8% (81.9-90.5%)
Negative Predictive Value (NPV)	64.6% (58.6-70.2%)
Positive Likelihood Ratio (+LR)	3.77 (2.59-5.48)
P value	<0.001

Original research

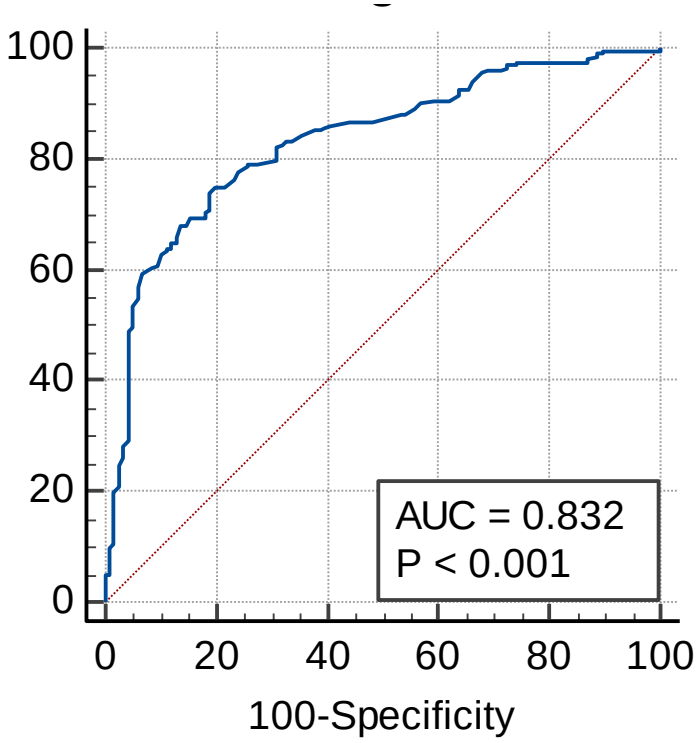

Fig 1. ROC Curve for the diagnostic ability of ALBI score to differentiate between chronic HCV patients (F3&F4) and healthy controls.

d) Subgroup analysis of ALBI score according to the liver fibrosis stage

The mean ALBI score for the F4 group was -2.3±0.62 (95% CI for the mean: -2.38 to -2.2), while it was -2.64±0.46 (95% CI for the mean: -2.89 to -2.39) for F3 group, (p-value <0.0001) as shown in **Figure (2)**. The ROC curve for the prognostic ability of the ALBI score to differentiate F3 from F4 revealed an AUROC = 0.654 (95% CI: 0.584 to 0.720) (p-value=0.02), as shown in **Figure (3).**

Original research

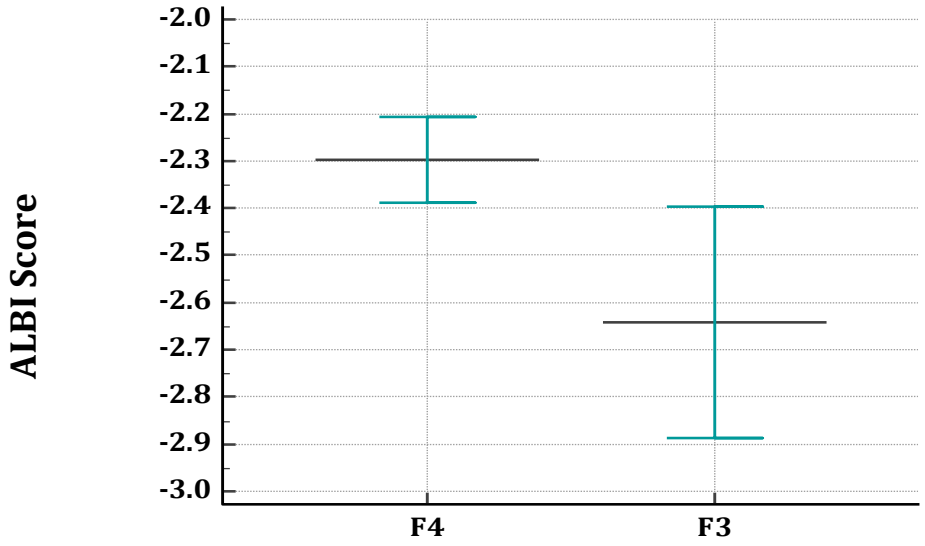

Fig 2. Comparison of the ALBI score's mean (95% CI) in F3 and F4 chronic HCV cases.

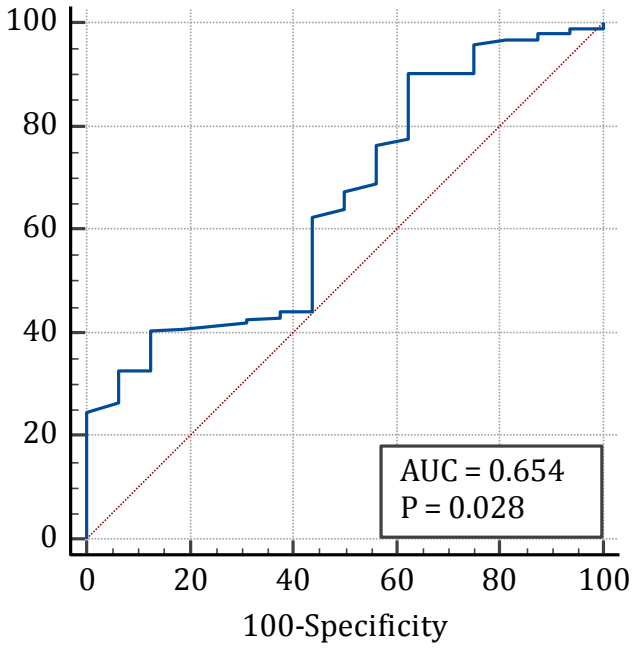

Fig 3. ROC Curve for the diagnostic ability of ALBI score to differentiate between F3 and F4 for chronic HCV cases.

Original research

Discussion

Several research studies have shown that the ALBI score is superior to other commonly used liver function assessment scores [11, 12]. In addition, it has been widely studied as a predictor of survival in patients with HCC [13, 14]. However, it has not been thoroughly investigated as a non-invasive indicator of advanced liver fibrosis and cirrhosis. Therefore, we conducted this study to explore the ability of the ALBI score to distinguish patients with advanced stages of liver fibrosis and cirrhosis (F3 and F4) from healthy controls.

The current study revealed that the ALBI score, as a predictor of advanced liver fibrosis and cirrhosis (F3 and F4) in comparison to healthy controls, had an AUROC of 0.832 (95% CI: 0.787-0.872), the sensitivity of 74.8%, specificity of 80.2%, PPV of 86.8%, NPV of 64.6%, and positive likelihood ratio of 3.77. The cut-off value to differentiate F3 and F4 chronic HCV patients from healthy controls was -2.781.

Our findings are consistent with those of Fujita et al. [15]. They studied the ability of the ALBI score to distinguish advanced liver fibrosis [F3-F4] from non-advanced fibrosis [F1-F2] in a cohort of chronic HCV patients. They reported an AUROC of 0.815, a sensitivity of 73.2%, a specificity of 87.1%, a positive likelihood ratio of 5.67, and a cut-off value of -2.125 to differentiate F3-F4 from F1-F2.

Our results are also in harmony with another study conducted by Fujita et al. to investigate the ability of ALBI score to differentiate liver fibrosis stage in patients with chronic hepatitis B infection. According to Fujita et al., the ALBI score determined the cirrhotic stage (F4) from the non-cirrhotic stage (F1-F3). They reported an AUROC of 0.849, sensitivity=85.7%, specificity=74%, a positive likelihood ratio of 3.30, and a cut-off value of -2.190 for differentiating F4 from F 1–3 [16]. In addition, they also found that the ALBI score could differentiate F4 from F3 (P-value < 0.05).

The current study found that the ALBI score, as a non-invasive marker of advanced liver fibrosis (F3) and cirrhosis (F4), was comparable to other conventional non-invasive

biomarkers, such as the APRI score. According to a meta-analysis of 40 studies including (n=8,739) HCV patients, the APRI score had an AUROC of 0.80 for the diagnosis of severe liver fibrosis (F3) and 0.83 for the diagnosis of cirrhosis [17]. Another meta-analysis of 22 studies that included (n = 4,266) patients found that the summary AUROCs of APRI for diagnosis of severe liver fibrosis were 0.76 [95% CI: 0.74 to 0.79] and 0.82 [95% CI: 0.79 to 0.85] for diagnosis of established liver cirrhosis, with an APRI threshold of 0.5 providing 81% sensitivity and 50% specificity [18].

Our findings also revealed that the ALBI score was comparable to the conventional FIB-4 test. According to Amorim et al., the FIB-4 test has an AUROC of 0.8±0.04 for diagnosing severe fibrosis in HCV patients [19]. Martin et al. found that the FIB-4 test had an AUROC of 0.73 (95 % CI 0.68-0.78) in cirrhotic patients [20].

In the context of limited resources, the World Health Organization (WHO) guidelines for diagnosis and staging of hepatic fibrosis [21] suggested that simple non-invasive serological markers rather than expensive tests that require extensive resources, such as TE or Fibro-test, should be used for the evaluation of hepatic fibrosis [22].

Implications of the study: our findings implicate that the application of the ALBI score could be broadened from the prognosis of liver cirrhosis and HCC to differentiating patients with advanced liver fibrosis and cirrhosis from non-cirrhotic individuals. ALBI score could be employed in the primary care setting.

Limitation of the study: (1) Limited sample size **(2)** Percutaneous liver biopsy, as a standard gold test, was not performed for the chronic HCV patients for confirmation and staging of hepatic fibrosis, **(3)** Although the abdominal ultrasound was unremarkable alongside negative laboratory and viral markers, we were unable to completely exclude any underlying liver pathology in the healthy individuals and were unable to perform TE for this group due to limited resources.

Conclusion: ALBI scores could significantly differentiate between chronic HCV patients with advanced liver fibrosis and cirrhosis from healthy controls. In addition, the ALBI

score could distinguish between (F3) and (F4) cases. Implementing ALBI score in the primary care may allow for earlier management and reduced liver-related morbidity and mortality.

Future perspectives: Future studies with a larger sample size to explore the predictive ability of the ALBI score to distinguish different liver fibrosis stages are recommended.

List of abbreviations

AFP: Alfa-fetoprotein, **ALBI:** Albumin Bilirubin, **APRI:** AST to Platelets Ratio Index**, AUROC:** Area Under Receiver Operating Characteristic, **ALT:** Alanine Transaminase, **AST:** Aspartate Transaminase, **CI:** Confidence Interval, **CT:** Computed Tomography, **DAAs:** Direct Acting Antivirals, **FBC:** Full Blood Count**, FIB-4:**Fibrosis-4, **HBsAg:** Hepatitis B surface Antigen, **HB:** Hemoglobin**, HCC:** Hepatocellular Carcinoma, **HCV:** Hepatitis C Virus, **kPa:** Kilo-Pascal**, MRI:** Magnetic Resonance Imaging, **PCR:** Polymerase Chain Reaction, **ROC:** Receiver Operating Characteristic, **SD:** Standard Deviation, **TE:** Transient Elastography, **WBCs:** White Blood Cells.

Authors' Contribution:

Dina M. Ali is the principal investigator responsible for the concept, study design, data collection, data analysis and interpretation, writing the draft, and critical revision of the final manuscript. Mohamed A. AlMoslemany & Osama Mohamed are attributed to the interpretation of data. Khaled Raafat is attributed to critical revision of the final manuscript for the intellectual content.

Funding source: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data availability: The corresponding author will supply the data supporting the study's findings upon reasonable request.

Original research

Conflict of interest: There are no potential conflicts of interest for the authors to disclose.

Footnotes.

Peer-Reviewers: Marwa Shabana (assistant professor of clinical pathology), Ahmed Gad (lecturer of internal medicine), Amr Shaban (professor of internal medicine), Ahmed Agrodey (assistant professor of internal medicine), Bassam Mansour (lecturer of tropical medicine).

E- Editor: Salem Youssef Mohamed.

Copyright ©. This open-access article is distributed under the Creative Commons Attribution License (CC BY). The use, distribution, or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited. The original publication in this journal is cited by accepted academic practice. No use, distribution, or reproduction is permitted, complying with these terms.

Disclaimer: All claims expressed in this article are solely those of the authors and do not necessarily represent their affiliated organizations or those of the publisher, the editors, and the reviewers. Any product evaluated in this article or its manufacturer's claim is not guaranteed or endorsed by the publisher.

References

1. Williams R, Aspinall R, Bellis M. Lancet Commission. Addressing the crisis of liver disease in the UK: a blueprint for attaining excellence in healthcare for liver disease and reducing premature mortality from the major lifestyle issues of excess alcohol consumption, obesity and viral. Lancet 2014; 384:1953–97.
2. D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. J Hepatol. 2006; 44:217–231.

3. Hydes T, Moore M, Stuart B, et al. Can routine blood tests be modeled to detect advanced liver disease in the community: model derivation and validation using UK primary and secondary care data. BMJ Open. 2021 Feb 11; 11(2):e044952.
4. Baranova A, Lal P, Birerdinc A, Younossi ZM. Non-invasive markers for hepatic fibrosis. BMC Gastroenterol. 2011 Aug 17; 11:91.
5. Chin JL, Pavlides M, Moolla A, Ryan JD. Non-invasive markers of liver fibrosis: adjuncts or alternatives to liver biopsy? Front Pharmacol. 2016 Jun 20; 7:159.
6. Papadopoulos N, Vasileiadi S, Papavdi M, et al. Liver fibrosis staging with a combination of APRI and FIB-4 scoring systems in chronic hepatitis C as an alternative to transient elastography. Ann Gastroenterol. 2019; 32:498–503.
7. Li Q, Chen T, Shi N, Ye W, Yuan M, Shi Y. Quantitative evaluation of hepatic fibrosis by fibro Scan and Gd-EOB-DTPA-enhanced T1 mapping magnetic resonance imaging in chronic hepatitis B. Abdom Radiol (NY). 2022 Feb; 47(2):684-692.
8. Deng M, Ng SWY, Cheung ST, Chong CCN. Clinical application of Albumin-Bilirubin (ALBI) scores: the current status. Surgeon. 2020 Jun; 18(3):178-186.
9. Bonder A, Afdhal N. Utilization of FibroScan in clinical practice. Curr Gastroenterol Rep. 2014 Feb; 16(2):372.
10. Johnson PJ, Berhane S, Kagebayashi C, et al. Assessment of liver function in patients with hepatocellular carcinoma: a new evidence-based approach-the ALBI grade. J Clin Oncol. 2015 Feb 20; 33(6):550-8.
11. Lei Q, Zhang Y, Ke C, et al. Value of the albumin-bilirubin score in evaluating hepatitis B virus-related acute-on-chronic liver failure, liver cirrhosis, and hepatocellular carcinoma. Exp Ther Med. 2018 Mar; 15(3):3074-3079.
12. Si-Zhe Wan, Yuan Nie, Yue Zhang, Cong Liu, Xuan Zhu. Assessing the prognostic performance of the Child-Pugh Model for End-Stage Liver Disease, and Albumin-Bilirubin scores in patients with decompensated cirrhosis: A large Asian cohort from gastroenterology department. Dis Markers. 2020 Feb 15; 2020:5193028.

13. Tada T, Kumada T, Toyoda H, et al. Impact of albumin-bilirubin grade on survival in patients with hepatocellular carcinoma who received sorafenib: an analysis using time-dependent receiver operating characteristic. J Gastroenterol Hepatol. 2019 Jun; 34(6):1066-1073.
14. Peng Y, Wei Q, He Y, et al. ALBI versus child-pugh in predicting the outcome of patients with HCC: A systematic review. Expert Rev Gastroenterol Hepatol. 2020 May; 14(5):383-400.
15. Fujita K, Oura K, Yoneyama H, et al. Albumin-bilirubin score indicates liver fibrosis staging and prognosis in patients with chronic hepatitis C. Hepatol Res. 2019 Jul;49(7):731-742.
16. Fujita K, Nomura T, Morishita A, et al. Albumin-Bilirubin score differentiates liver fibrosis stage and hepatocellular carcinoma incidence in chronic hepatitis B virus infection: A retrospective cohort study. Am J Trop Med Hyg. 2019 Jul;101(1):220-225
17. Lin ZH, Xin YN, Dong QJ, et al. Performance of the aspartate aminotransferase-to-platelet ratio index for staging hepatitis C-related fibrosis: an updated meta-analysis. Hepatology. 2011; 53:726–736.
18. Shaheen AA, Myers RP. Diagnostic accuracy of the aspartate aminotransferase-to-platelet ratio index for the prediction of hepatitis C-related fibrosis: a systematic review. Hepatology. 2007; 46:912–921.
19. Amorim TG, Staub GJ, Lazzarotto C, et al. Validation and comparison of simple noninvasive models for the prediction of liver fibrosis in chronic hepatitis C. Ann Hepatol. 2012 Nov-Dec; 11(6):855-61.
20. Martin J, Khatri G, Gopal P, Singal AG. Accuracy of ultrasound and noninvasive markers of fibrosis to identify patients with cirrhosis. Dig Dis Sci. 2015; 60:1841–1847.
21. World Health Organization. (2016). Guidelines for the screening, care and treatment of persons with chronic hepatitis C infection, updated version, April

2016. World Health Organization. https://apps.who.int/iris/handle/10665/205035 (Accessed November 7th, 2022).

22. Poynard T, Imbert-Bismut F, Munteanu M, et al. Overview of the diagnostic value of biochemical markers of liver fibrosis (FibroTest, HCV FibroSure) and necrosis (ActiTest) in patients with chronic hepatitis C. Comp Hepatol 2004 Sep 23;3(1):8.