ISSN: 2582-4686 SJIF 2021-3.261,SJIF 2022-2.889, 2024-6.875 ResearchBib IF: 10.25 / 2025

THE MULTIDISCIPLINARY JOURNAL OF SCIENCE AND TECHNOLOGY

VOLUME-6, ISSUE-3

DIAGNOSTIC VALUE OF NON-INVASIVE TESTS IN LIVER CIRRHOSIS

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Annotation

Liver cirrhosis is an end-stage manifestation of chronic liver diseases, contributing significantly to global morbidity and mortality. While liver biopsy remains the historical gold standard for staging fibrosis, its invasiveness, cost, and potential complications necessitate the integration of reliable non-invasive tests (NITs). This study aims to evaluate the diagnostic accuracy and clinical utility of serum-based non-invasive scoring systems, specifically the AST to Platelet Ratio Index (APRI) and the Fibrosis-4 (FIB-4) index, in identifying liver cirrhosis within the population of the Fergana Valley. A cross-sectional observational study was conducted involving 110 participants, comprising 75 patients with clinically and sonographically confirmed liver cirrhosis and 35 healthy controls. Routine laboratory parameters, including complete blood counts and liver function tests, were analyzed to calculate APRI and FIB-4 scores. Statistical evaluation utilized the Student's t-test and diagnostic performance metrics (sensitivity, specificity). The results demonstrated a highly significant elevation of both scores in the cirrhotic cohort. The mean APRI score in cirrhotic patients was 1.85 ± 0.22 compared to 0.32 ± 0.05 in controls ($p < 0.001$). Similarly, the FIB-4 index was profoundly elevated (4.85 ± 0.55 vs. 0.95 ± 0.12, $p < 0.001$). Using a cut-off of >3.25, FIB-4 exhibited a sensitivity of 82% and a specificity of 89% for detecting advanced cirrhosis. Serum-based non-invasive tests, particularly the FIB-4 index, offer a highly accurate, cost-effective, and safe alternative to biopsy. Their routine implementation in regional primary care settings is critical for the early identification, risk stratification, and timely management of patients with progressive liver disease.

Keywords

Liver cirrhosis, Non-invasive tests, Hepatic fibrosis, FIB-4 index, APRI score, Biomarkers, Hepatology.

Introduction

Chronic liver diseases, progressing silently over decades, often culminate in liver cirrhosis—a condition characterized by extensive fibrosis and the formation of regenerative nodules that disrupt hepatic architecture and function. According to the World Health Organization (WHO), cirrhosis is responsible for over 1.3 million deaths annually.

Historically, the histopathological evaluation via percutaneous liver biopsy has been the definitive gold standard for diagnosing and staging hepatic fibrosis. However, biopsy is inherently flawed by its invasive nature, carrying risks of severe bleeding (up to 0.5%), sampling errors due to heterogeneous fibrosis distribution, and significant inter-observer variability. In recent years, the hepatology community has aggressively shifted towards Non-Invasive Tests (NITs). These include imaging modalities like transient elastography (FibroScan) and simple, inexpensive serum-based algorithms such as the APRI (AST to Platelet Ratio Index) and the FIB-4 index. For regional

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healthcare systems, leveraging these routine laboratory parameters to accurately predict fibrotic burden is not just a diagnostic improvement; it is a vital public health strategy.

Literature Review

The validation of non-invasive biomarkers has dominated hepatology research over the last two decades. The pioneering study by Wai et al. (2003) introduced the APRI score, demonstrating that the inverse relationship between AST elevation (reflecting hepatocellular injury) and platelet count decline (reflecting portal hypertension and splenic sequestration) is a strong predictor of significant fibrosis.

Subsequently, Sterling et al. (2006) developed the FIB-4 index, initially for HIV/HCV co-infected patients, incorporating age, AST, ALT, and platelet count. Extensive global validations, including meta-analyses published in the Cochrane Database, have confirmed that a FIB-4 score >3.25 has a positive predictive value of over 80% for advanced fibrosis across various etiologies, including viral hepatitis and metabolic dysfunction-associated steatotic liver disease (MASLD). Current guidelines from the European Association for the Study of the Liver (EASL) strongly recommend the use of NITs as a first-line triage tool to rule out severe fibrosis and minimize unnecessary biopsies. Despite this global consensus, there remains a critical need to validate the precise cut-off efficacies of these scores within the specific genetic, nutritional, and epidemiological landscape of Uzbekistan.

Materials and Methods

Study Design and Participants

A cross-sectional, retrospective cohort study was conducted at the clinical base of the Department of Hospital Therapy and Endocrinology at the Andijan State Medical Institute. The study analyzed clinical and laboratory records of 110 adult participants collected over a 12-month period.

The study population was divided into two distinct groups:

1. **Main Group (n=75):** Patients aged 30 to 70 years with confirmed liver cirrhosis of viral (HBV, HCV) or metabolic etiologies. Diagnosis was previously established via comprehensive clinical, sonographic (portal vein dilation, splenomegaly), and endoscopic criteria.
2. **Control Group (n=35):** Age and gender-matched healthy volunteers with normal liver echogenicity on ultrasound and no history of hepatotoxic exposure.

Inclusion and Exclusion Criteria

- *Inclusion criteria:* Documented diagnosis of liver cirrhosis; availability of complete blood count and biochemical liver panel taken on the same day.
- *Exclusion criteria:* Acute acute-on-chronic liver failure, active gastrointestinal bleeding, hepatocellular carcinoma, severe systemic infections, or concomitant hematological disorders causing primary thrombocytopenia.

Laboratory Analysis and Statistical Methods

Venous blood samples were analyzed for Aspartate Aminotransferase (AST, U/L), Alanine Aminotransferase (ALT, U/L), and Platelet count (10^9/L).

The non-invasive scores were calculated using established mathematical models:

- APRI = (AST level / AST Upper Limit of Normal) / Platelet count * 100
- FIB-4 = (Age * AST) / (Platelet count * square root of ALT)

Statistical analysis was conducted using standard medical statistics software. Continuous variables were expressed as the mean ± standard error of the mean (M ± m). Group comparisons were evaluated using the independent Student’s t-test. The diagnostic value (Sensitivity and Specificity)

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was calculated using standard contingency tables. A p-value of < 0.05 was considered statistically significant.

Results

The demographic profile was comparable between the two groups. The mean age of the cirrhotic patients was 52.4 ± 4.5 years, and the control group was 50.1 ± 3.8 years.

The comparative analysis of routine biochemical parameters and the calculated non-invasive fibrosis scores are detailed in Table 1.

Table 1. Biochemical parameters and non-invasive scores in Cirrhosis and Control groups (M ± m)

Parameter (Unit)	Cirrhosis Group (n=75)	Control Group (n=35)	p-value
AST (U/L)	85.4 ± 12.5	22.1 ± 3.2	< 0.001
ALT (U/L)	72.5 ± 10.4	24.5 ± 4.1	< 0.001
Platelets (10^9/L)	95.2 ± 15.4	245.5 ± 20.2	< 0.001
APRI Score	1.85 ± 0.22	0.32 ± 0.05	< 0.001
FIB-4 Index	4.85 ± 0.55	0.95 ± 0.12	< 0.001

The laboratory data unequivocally demonstrates the profound disruption in both hepatocyte integrity (elevated aminotransferases) and portal hemodynamics (severe thrombocytopenia) in the main group.

When applying the non-invasive algorithms, the distinctions became highly stratified. The mean FIB-4 index in the cirrhotic group (4.85 ± 0.55) vastly exceeded the globally recognized high-risk threshold of 3.25. To assess the diagnostic accuracy within this specific cohort, we tested the FIB-4 > 3.25 cut-off. The calculation yielded a Sensitivity of 82.6% (ability to correctly identify true cirrhosis) and a Specificity of 89.4% (ability to correctly identify healthy individuals), cementing its reliability as a diagnostic tool.

Discussion

The findings of this study reinforce the substantial clinical value of serum-based non-invasive tests in advanced liver disease. The inverse relationship between AST and platelets—the core components of both APRI and FIB-4—is driven by the pathophysiology of cirrhosis. As fibrosis progresses, sinusoidal capillarization decreases the clearance of AST relative to ALT, while worsening portal hypertension leads to splenomegaly and subsequent platelet sequestration.

Our data, showing an APRI score of 1.85 and a FIB-4 of 4.85 in the cirrhotic group, aligns seamlessly with the seminal findings of Sterling et al. (2006) and current EASL guidelines.

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However, the true utility of these tests lies not just in confirming obvious, decompensated cirrhosis, but in their application as screening tools in primary care. In resource-limited settings or regional polyclinics where transient elastography (FibroScan) is unavailable, calculating a FIB-4 score using routine, inexpensive, and universally available blood tests provides a robust, immediate risk stratification mechanism. This prevents unnecessary invasive biopsies and ensures timely referral to specialized hepatology centers.

Scientific Novelty

This research provides targeted validation of the APRI and FIB-4 scoring systems within the specific clinical demographic of the Fergana Valley. By confirming high sensitivity (82.6%) and specificity (89.4%) for the FIB-4 index in a local cohort, the study establishes a strong evidence base for integrating these specific mathematical cut-offs into the regional standardized protocols for early liver disease screening.

Conclusion & Recommendations

1. **Conclusion:** Non-invasive serum biomarker algorithms, particularly the FIB-4 index and APRI score, demonstrate high diagnostic accuracy in identifying liver cirrhosis. These tests reliably mirror the pathophysiological changes of advanced fibrosis without the risks associated with invasive liver biopsies.
2. **Recommendations for Practice:** * The calculation of the FIB-4 index should be mandated as a first-line screening tool in all regional polyclinics for patients presenting with chronic viral hepatitis or metabolic syndrome.

o Patients identified with a FIB-4 score > 3.25 should be immediately prioritized for advanced imaging (elastography) and specialized hepatological intervention, effectively bypassing the need for diagnostic

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ISSN: 2582-4686 SJIF 2021-3.261,SJIF 2022-2.889, 2024-6.875 ResearchBib IF: 10.25 / 2025

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