

Serum Golgi Protein 73 as a Noninvasive Biomarker for Assessing Liver Diseases in a Tertiary Care Hospital

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Abstract

Background

Chronic liver disease (CLD) and fatty liver disease (FLD) are major public health concerns in Nepal and may progress to fibrosis, cirrhosis, and hepatocellular carcinoma. Conventional liver function tests are widely used for disease evaluation but have limited specificity for assessing disease progression. Golgi protein 73 (GP73) has evolved as a promising biomarker for detecting hepatocellular injury and evaluating the severity of liver disease. Our study aims to evaluate the diagnostic utility of serum GP73 levels in predicting the progression or severity of liver disease among patients with fatty liver disease and chronic liver disease in a tertiary care setting.

Methods

Participants were categorized according to findings based on ultrasonography in this prospective single-center cross-sectional study. Serum GP73 levels were measured using an automated chemiluminescence immunoassay. The diagnostic performance of GP73 was compared with conventional liver function tests and noninvasive markers such as aspartate aminotransferase-to-platelet ratio index (APRI) and Fibrosis-4 (FIB-4) index. Receiver operating characteristic curve analysis was performed to assess diagnostic accuracy.

Results

Among the 85 participants, 52(61.18%) had fatty liver disease grade 1 (FLG1), 23(27.06%) had fatty liver disease grade 2 (FLG2), and 10(11.76%) had CLD. Serum GP73 levels increased significantly with increasing disease severity ($p < 0.001$). Median GP73 levels were markedly higher in patients with FLG2 and CLD compared to those with FLG1 (59.10 ng/mL [36.15–158.00] vs. 36.70 ng/mL [26.70-55.82], $p < 0.001$). GP73 demonstrated excellent diagnostic performance for distinguishing CLD and FLG2 from FLG1, with an area under the curve (AUC) of 0.856 ($p < 0.001$) at a cutoff value of 110 ng/mL, outperforming both the FIB-4 index (AUC = 0.827) and APRI score (AUC = 0.757).

Conclusions

Serum GP73 is an emerging noninvasive biomarker for identifying chronic liver disease and distinguishing early-stage fatty liver disease from more advanced hepatic disease like FLG2 and CLD. Its high diagnostic accuracy, particularly at a cutoff value of 110 ng/mL for CLD, suggests potential utility in clinical settings where liver biopsy, transient elastography, or FibroScan assessment are either unavailable or unaffordable. The combined use of GP73 with established fibrosis markers such as FIB-4 and APRI may further improve the assessment of liver fibrosis and cirrhosis.

Backgrounds

Liver disorders remain a major public health challenge worldwide, affecting a substantial proportion of the population and contributing significantly to morbidity and mortality [1]. If left untreated, hepatic injury may gradually advance from early pathological changes to fibrosis, cirrhosis, and ultimately hepatocellular carcinoma, releasing liver enzymes like aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and advanced up-regulated proteins [2–6]. Timely evaluation of disease stage is important for clinical decision-making, monitoring of patients, and prediction of outcomes [7, 8]. There is increasing interest in identifying biomarkers that can reliably assess liver disease without the need for invasive procedures [9]. Under physiological conditions, circulating golgi phosphoprotein-2 or golgi membrane protein-1 (GP73) levels remain low; however, hepatocellular stress and inflammatory injury stimulate its expression and release into the bloodstream [6, 10]. Rising serum GP73 concentrations have been linked to progressive hepatic fibrosis, cirrhosis, and hepatocellular malignancy [6, 11–18]. AST can rise during extrahepatic events like myocardial infarction, while ALP elevations often overlap significantly with bone pathology or independent extrahepatic obstructions [11]. Despite its established role in fibrosis assessment, liver biopsy has several practical limitations that restrict its routine use in clinical settings [2, 3]. Consequently, serum GP73 has emerged as a potential non-invasive diagnostic marker when compared to standard individual liver enzymes and non-invasive calculations, including the Fibrosis-4 (FIB-4) index and the aspartate aminotransferase-to-platelet ratio index (APRI) score [2, 3]. This study investigates the clinical diagnostic utility of serum GP73 in patients presenting with various liver diseases identified via ultrasound, representing the first assessment of this novel hepatobiliary biomarker within a tertiary care setting in southwestern Nepal.

Methods

This cross-sectional study was conducted in Universal College of Medical Sciences and Teaching Hospital (UCMSTH), Bhairahawa, Nepal, at the Departments of Biochemistry and Radiodiagnosis from August 2025 to Jan 2026. Using a purposive sampling technique, a total of 85 participants aged 30 years and older were enrolled over a six-month data collection period. Participants were categorized into two distinct cohorts based on clinical presentations and ultrasonographic findings. Cohort 1 included patients with fatty liver disease grade 2 (FLG2) and chronic liver disease (CLD). Cohort 2 included fatty liver disease grade 1 (FLG1). All liver diseases were evaluated using ultrasonography. Patients with a history of solid tumors (e.g., lung, prostate, gastric, colon, or breast cancers) or those undergoing specific antiviral treatments such as interferon therapy were excluded, as these factors independently alter serum Golgi protein 73 (GP73) levels. The sample size was determined using the formula for a quantitative variable, where the values of the parameters were obtained from a previously published study [19]. The minimum required sample size was calculated to be 42 participants. During the study period, 85 participants meeting the eligibility criteria were enrolled.

Data Collection and Clinical Evaluations Socio-demographic details, clinical histories, and hospital IDs were recorded on a structured study proforma. Physical measurements for weight and height were taken

using verified weighing scales and measuring tapes. A certified radiologist performed transabdominal ultrasound examinations using standardized protocols to evaluate liver pathology. Peripheral venous blood was drawn under aseptic conditions. Samples were collected in an EDTA tube for platelet (PLT) estimation, and a plain serum separator tube for the measurement of GP73, AST, ALT, and ALP. Samples were processed immediately after collection. For any unavoidable delays, EDTA blood samples were stored at 2–8 degrees Celsius, and serum samples were stored at -20 degrees Celsius. Frozen samples were thawed immediately before analytical evaluation. Platelet concentrations were measured using an automated hematology analyzer (Sysmex XN-550; Sysmex Corporation, Kobe, Japan) and cross-verified manually by peripheral blood smear (PBS) examinations. Quantitative estimation of serum GP73 was performed using a chemiluminescence immunoassay automated analyzer (MAGLUMI 2000; Snibe Diagnostic, Shenzhen, China). Serum AST, ALT, and ALP levels were measured via enzymatic methods using a fully automated clinical chemistry analyzer (P-500 DIATRON; Diatron, Budapest, Hungary).

Collected data were entered into Microsoft Excel 2010 and analyzed using the Statistical Package for the Social Sciences (SPSS) version 20.0 (IBM Corp., Armonk, NY, USA). Before formal analysis, dataset entries were audited for completeness, consistency, and accuracy. Categorical variables are measured as frequencies and percentages. Continuous variables were evaluated for normal distribution using the Shapiro-Wilk test. Because the laboratory biomarkers exhibited non-normal distributions, they are presented as medians and interquartile ranges (IQRs). For inferential statistics, differences and comparisons between two or more independent groups were assessed using the Mann-Whitney U test and Kruskal- Wallis test. Subsequent post hoc pairwise comparisons with appropriate adjustments were evaluated using the Wilcoxon signed-rank test. Receiver Operating Characteristic (ROC) curve analysis was used to measure the diagnostic accuracy of serum GP73, the APRI score, and the FIB-4 index. The area under the curve (AUC) and corresponding 95% confidence intervals (CI) estimated diagnostic cut-off values. Associated diagnostic performance indices such as sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), were calculated for each biomarker. Correlation analyses were computed using Spearman's rank correlation coefficient to assess the relationships between serum GP73 levels and biochemical or fibrosis-related parameters. All statistical analyses were conducted using two-sided tests, and statistical significance was defined as a p-value < 0.05.

Results

The majority of participants were Hindu, 79(92.94%), while 3 were Buddhists and 3 were Muslims, each accounting for 3.53% of the study population. Nearly half of the participants reported alcohol consumption, 42(49.41%), whereas smoking was reported by only 11(12.94%), indicating a predominantly non-smoking cohort. Overweight (pre- obese) individuals constituted the largest proportion of the study population, 31(36.47%), followed by those with normal weight, 28(25.53%). Obesity Classes I, II, and III were observed in 8(21.18%), 7(8.24%), and 5(5.88%) of participants, respectively, while 4(4.71%) were underweight (Table 1). Ascites and hepatic encephalopathy were infrequent findings, occurring in 3(3.53%) and 2(1.18%) of participants, respectively. Most subjects were non-reactive for viral markers 80(94.11%), with only a small proportion demonstrating HCV or HBsAg

positivity. According to the APRI score, 38(44.71%) of participants had no evidence of significant fibrosis, 24(28.24%) had findings suggestive of possible advanced fibrosis, 6(7.06%) had findings consistent with advanced fibrosis, and 17(20.00%) were classified as having cirrhosis. Based on the FIB-4 index, 39(45.88%) of participants were categorized as being at high risk for advanced fibrosis (Table 1). Ultrasonographic examination revealed that fatty liver disease was the predominant hepatic abnormality. Fatty liver disease grade 1 (FLG1) was the most common finding 52(61.18%), followed by fatty liver disease grade 2(FLG2) 23(27.06%). Chronic liver disease (CLD) was identified in 10(11.76%) of participants (Fig. 1).

Table 1
Demographic, Anthropometric, and Clinical profiles distribution of
the study population (N = 85)

Variables	Frequency
Religion	
Hindu	79(92.94%)
Buddhist	3(3.53%)
Muslim	3(3.53%)
Alcoholism	
Yes	42(49.41%)
No	43(50.59%)
Smoking	
Yes	11(12.94%)
No	74(87.66%)
Grading of BMI (Kg/m²)	
Normal Weight (18.5–24.9)	28(23.53%)
Overweight (Pre-obese) (25.0-29.9)	31(36.47%)
Obese Class I (Moderate) (30.0-34.9)	18(21.18%)
Obese Class II (Severe) (35.0-39.9)	7(8.24%)
Obese Class III (Very severe) (≥ 40.0)	5(5.88%)
Under Weight (< 18.5)	4(4.71%)
Ascites	
Yes	3(3.53%)
No	82(96.47%)
Hepatic Encephalopathy	
Yes	2(2.35%)
No	83(97.65%)
Serological Reactivity	
HCV Reactive	2(2.35%)
HBsAg Reactive	2(2.35%)

Variables	Frequency
HCV+ HBsAg Reactive	1(1.18%)
Non-Reactive	80(94.11%)
Category of APRI Score	
Rules Out Significant Fibrosis (< 0.5)	38(44.71%)
Suggestive Possible Advanced Fibrosis (0.5–1.5)	24(28.24%)
Suggestive Cirrhosis (1.6-2.0)	6(7.66%)
Diagnosis Of Cirrhosis (> 3.0)	17(20.00%)
Category of FIB-4 Index	
Low Risk of Advanced Fibrosis (< 1.3)	37(43.53%)
Intermediate Risk of Advanced Fibrosis (1.3–2.67)	9(10.59%)
High Risk of Advanced Fibrosis (> 2.67)	39(45.88%)

Total bilirubin, direct bilirubin, and indirect bilirubin levels increased significantly with disease severity ($P = 0.020$, $P = 0.005$, and $P = 0.022$, respectively), with the highest values observed in patient with CLD. AST levels differed significantly among groups ($P = 0.003$), whereas ALT levels did not show a significant difference ($P = 0.208$). The De Ritis ratio (AST/ALT) was significantly higher in participants with CLD and FLG2 compared with FLG1 ($P = 0.018$). No significant differences were observed in ALP or total serum protein levels across the study cohorts ($P = 0.104$ and $P = 0.277$). Serum albumin levels declined significantly with increasing disease severity ($P = 0.008$). Similarly, both APRI scores ($P = 0.006$) and FIB-4 indices ($P = 0.001$) increased significantly across disease categories, with the highest values observed in participants with CLD. Serum GP73 concentrations were significantly elevated in participants with liver disease and demonstrated a progressive increase with disease severity ($P = 0.001$) (Table 2).

Table 2
Liver function parameters in patients with liver diseases

Parameters	Liver Diseases		P-value
	CLD or FLG2 (95% CI)	FLG1 (95% CI)	
Total bilirubin (mg/dl)	1.40 (0.63–3.65)	0.86 (0.50–1.50)	0.020*
Direct bilirubin (mg/dl)	0.50 (0.29–2.50)	0.32 (0.21–0.57)	0.005*
Indirect bilirubin (mg/dl)	0.70 (0.34–1.40)	0.40 (0.24–0.87)	0.022*
AST (IU/L)	58 (35.50–118.50)	33 (23–54.25)	0.003*
ALT (IU/L)	42 (29.50–71.50)	37 (23.25–61.50)	0.208
De-ritis ratio	1.31 (0.85–2.35)	0.91 (0.69–1.33)	0.018*
ALP (IU/L)	96 (70–123.50)	82 (60–96.75)	0.104
Total protein (g/dl)	7.20 (6.30–8.00)	7.50 (6.92–7.90)	0.277
Albumin (g/dl)	3.80 (3.00–4.65)	4.45 (4.10–4.97)	0.008*
APRI score	0.91 (0.41–2.90)	0.42 (0.25–1.10)	0.006*
FIB-4 index	2.84 (1.74–8.40)	1.31 (0.71–2.90)	0.001*
Serum GP-73 (ng/ml)	59.10 (36.15–158.00)	36.70 (26.70–55.82)	0.001*
AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; APRI, AST-to-platelet ratio index; FIB-4, Fibrosis-4 index; GP-73, Golgi protein 73 De Ritis ratio = AST/ALT; ARPI score={ (AST/AST) ×100 }/platelet count; FIB-4 Index= (Age × AST) / (Platelet count × √ALT). Values are presented as median (interquartile range), *P < 0.05			

The APRI score was notably higher in the CLD group than in the FLG1 (P = 0.004). The FIB-4 index showed significant differences in all pairwise comparisons, being higher in CLD compared with FLG1 (P < 0.001) and FLG2 (P = 0.010), and also differing between FLG1 and FLG2 (P = 0.020). Analysis of serum GP73 levels using the Wilcoxon signed-rank test demonstrated significant differences between FLG1 and FLG2 (P = 0.030), grade 2 FLD and CLD (P = 0.006), and FLG1 and CLD (P < 0.001), indicating progressive elevation of GP73 with increasing disease severity (Fig. 2).

Serum GP73 showed the best diagnostic performance, with an AUC of 0.856 (P < 0.001) for differentiating CLD and FLG2 from FLG1. At a cutoff of 110 ng/mL, GP73 yielded a sensitivity of 80.00%, specificity of 88.00%, and an NPV of 97.05%. The FIB-4 index also performed well (AUC = 0.827, P = 0.001), whereas the APRI score showed moderate diagnostic accuracy (AUC = 0.757, P = 0.008), as demonstrated in Table 3 and Fig. 3.

Table 3

Diagnostic performance of GP73, APRI score, and FIB-4 index in differentiating **CLD** and **FLG2** from **FLG1**

Parameter	AUC	P-Value	95% CI	Cutoff Value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
GP73	0.856	< 0.001*	0.765–0.947	110	80.00	88.00	47.05	97.05
APRI Score	0.757	0.008*	0.636–0.879	0.694	90.00	62.66	24.32	97.91
FIB-4 Index	0.827	0.001*	0.724–0.929	4.81	80.00	84.00	40.00	96.92

***P < 0.05**

Serum GP73 levels showed significant positive correlations with total bilirubin, direct and indirect bilirubin, AST, ALP, De Ritis ratio, APRI score, and FIB-4 index ($P < 0.001$). A weak positive correlation was observed with ALT; however, this association was not statistically significant. Conversely, GP73 demonstrated significant negative correlations with serum albumin, total protein, and platelet count ($P < 0.001$). GP73 levels were not significantly associated with BMI ($P = 0.163$) (Table 4).

Table 4
The Correlation of serum GP73 levels with liver function parameters, fibrotic indices, platelets, and BMI (N = 85)

Parameters	Correlation coefficient (r)	P-Value
Total bilirubin	0.659	< 0.001*
Direct bilirubin	0.710	< 0.001*
Indirect bilirubin	0.336	0.001*
AST	0.633	< 0.001*
ALT	0.092	0.402
ALP	0.523	< 0.001*
De-ritis ratio	0.642	< 0.001*
Albumin	-0.606	< 0.001*
Total protein	-0.459	< 0.001*
FIB-4 Index	0.592	< 0.001*
APRI Score	0.629	< 0.001*
Platelet	-0.479	< 0.001*
BMI	-0.152	0.163

***P < 0.05**

Discussion

Studies have reported elevated circulating GP73 levels in association with increasing fibrosis burden and chronic liver injury, suggesting that GP73 reflects ongoing hepatocellular damage and disease progression [18–20]. Our study also examined the diagnostic performance of serum Golgi protein 73 (GP73) across varying stages of hepatic disorders, from fatty liver disease (FLD) grades to chronic liver disease (CLD) assessed by ultrasonography. In our cohort, age differed significantly across clinical groups ($p = 0.008$), with a higher median age of 55 years observed in patients with active liver disease. Older participants tended to exhibit more advanced liver disease, which may reflect the cumulative impact of long-term hepatic injury [12]. Conversely, body mass index (BMI) showed no significant difference between severity groups ($p = 0.626$). This observation is consistent with evidence indicating that liver disease may occur even in individuals with relatively low BMI in South Asian populations [13]. While the male-to-female ratio (1.17:1) was not statistically significant, males demonstrated relatively higher median GP73 levels, APRI scores, and FIB-4 values, indicating greater fibrosis-related risks. This

finding aligns with observed gender trends, with elevated GP73 expression noted in patients with progressive liver fibrosis, particularly among males with advanced liver disease [19].

Platelet counts demonstrated a decreasing trend with worsening disease severity, though without overall statistical significance across all groups ($p = 0.069$) in this study. However, pairwise comparison between fatty liver disease grade 1 (FLG1) and CLD revealed a significant drop in platelet counts in chronic cases ($p = 0.03$). A decline in platelet count is commonly observed with increasing fibrosis severity and is frequently used as an indirect marker of advanced liver disease [14]. Standard liver function parameters showed significant elevations in total, direct, and indirect bilirubin (1.40 mg/dL, $p = 0.020$; 0.50 mg/dL, $p = 0.005$; 0.70 mg/dL, $p = 0.022$, respectively) and AST levels (58 IU/L, $p = 0.003$) in liver disease patients in our study. Higher bilirubin concentrations may reflect deterioration in hepatic function and reduced efficiency of bilirubin processing and excretion [15]. Notably, AST rose prominently while ALT ($p = 0.208$) and ALP ($p = 0.104$) modifications remained non-significant. Although ALT is widely regarded as a marker of hepatocellular injury, AST may become more prominent in advanced stages of liver damage [16]. Consequently, the De Ritis ratio (AST/ALT) was highly significant for diagnosing severity ($p = 0.018$); an elevated ratio has been linked to more severe hepatic fibrosis and chronic liver disease in previous studies [14, 16]. Non-significant ALT and ALP findings indicate that markers of acute inflammation or cholestasis may be less sensitive in this cohort than indicators of chronic metabolic damage [15]. Furthermore, serum albumin levels were significantly reduced in liver disease patients (3.80 g/dL, $p = 0.008$), demonstrating impaired hepatic synthetic function—a hallmark of progressive CLD reflecting diminished functional hepatocytes [14, 15].

7 of 10 Non-invasive fibrosis markers, the APRI score ($p = 0.006$) and the FIB-4 index ($p = 0.001$), were significantly higher in fatty liver disease grade 2 (FLG2) and CLD, confirming their utility as dependable, cost-effective staging tools as in previous studies [16, 17]. The stronger statistical significance of the FIB-4 index matches global literature indicating that incorporating age and more thorough biochemical inputs yields superior diagnostic accuracy over the APRI score [16, 18]. Our analysis also demonstrated a direct positive association between serum GP73 levels and advancing hepatic fibrosis stages, matching historical work validating GP73 as a strong marker for substantial cirrhosis and fibrosis [21–23]. A key observation of the present study was the gradual increase in serum GP73 concentrations with increasing disease severity ($p < 0.001$). Median GP73 levels were significantly higher in CLD and FLG2 patients overall compared to FLG1 (59.10 ng/mL vs. 36.70 ng/mL, $p = 0.001$). This direct link with transaminases and inverse relationship with albumin supports GP73 as a highly sensitive biomarker for monitoring hepatic dysfunction [20, 24]. These findings echo historical data where serum GP73 concentrations correlate strongly with histological fibrosis stages and cirrhosis, frequently outperforming traditional indices [3, 8, 20]. When combined with other blood indicators like Golgi Protein 73, these non-invasive indices provide accurate method of assessing the course of liver disease, potentially reducing the need for invasive procedures like liver biopsy for fibrosis staging [5, 6, 23].

Receiver operating characteristic (ROC) analysis demonstrated that GP73 exhibited diagnostic accuracy with an AUC of 0.856 ($p < 0.001$) at a cut-off of 110 ng/mL, sensitivity 80% and specificity 88%. Crucially,

the negative predictive value was remarkably high (97.05%). In this analysis, GP73 outperformed both the APRI score (AUC = 0.757) and the FIB-4 index (AUC = 0.827), matching previous study showing that GP73 has high diagnostic accuracy for advanced fibrosis and cirrhosis [25]. Among the evaluated biomarkers, GP73 achieved the highest overall discriminatory performance, demonstrating favorable sensitivity, specificity, and an excellent negative predictive value at the identified cutoff concentration. Although both APRI and FIB-4 also showed diagnostic utility, GP73 provided superior overall classification accuracy within this study population. These findings suggest that GP73 may be particularly valuable for identifying individuals who are unlikely to have advanced liver disease and may therefore reduce reliance on more invasive or less accessible diagnostic procedures like liver biopsy.

Study Limitations

This study is subject to certain limitations that should be considered. First, liver biopsy, the clinical gold standard for fibrosis staging, was not performed for direct histopathological correlation with serum biomarker levels. Second, the cross-sectional design of this study precludes the evaluation of GP73 as a long-term prognostic marker or predictor of longitudinal disease progression over time. Future longitudinal studies featuring larger cohorts and direct histological confirmation are warranted to further validate GP73 as a routine clinical biomarker.

Conclusions

Increasing serum GP73 concentrations were observed across the spectrum of hepatic disease evaluated in this study, with the highest levels detected among participants with chronic liver disease. The biomarker demonstrated good discriminatory ability for distinguishing more advanced hepatic involvement from early-stage fatty liver disease and performed favorably when compared with established non-invasive fibrosis indices like APRI and FIB-4. These findings support the potential role of GP73 as an adjunctive tool for liver disease assessment, particularly in settings where advanced imaging modalities or histopathological evaluation are not readily available. Further multicenter studies with larger sample sizes and histological validation are required to establish its routine clinical application.

Declarations

Acknowledgments

None

Conflict of Interest / Competing Interests

None

Funding

None

Data Availability Statement

Data can be made available on request to corresponding author

Consent to Participate

Written informed consent was obtained from all participants prior to enrollment in the study.

Ethical Approval / Ethics Statement

Ethical clearance for this study was approved by Institutional Review Committee of Universal College of Medical Sciences, Nepal with Approval number 126/25.

Author Contributions

Acquisition, analysis, or interpretation of data: P.P., N.G., S.D., S.R., J.S., B.T., B.K.S., and B.K.

Drafting of the manuscript: P.P., N.G., S.D., S.R., B.R.P., B.K.S., and S.G.

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Concept and design: N.G., S.D., B.R.P., S.G., and P.R.

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Figures

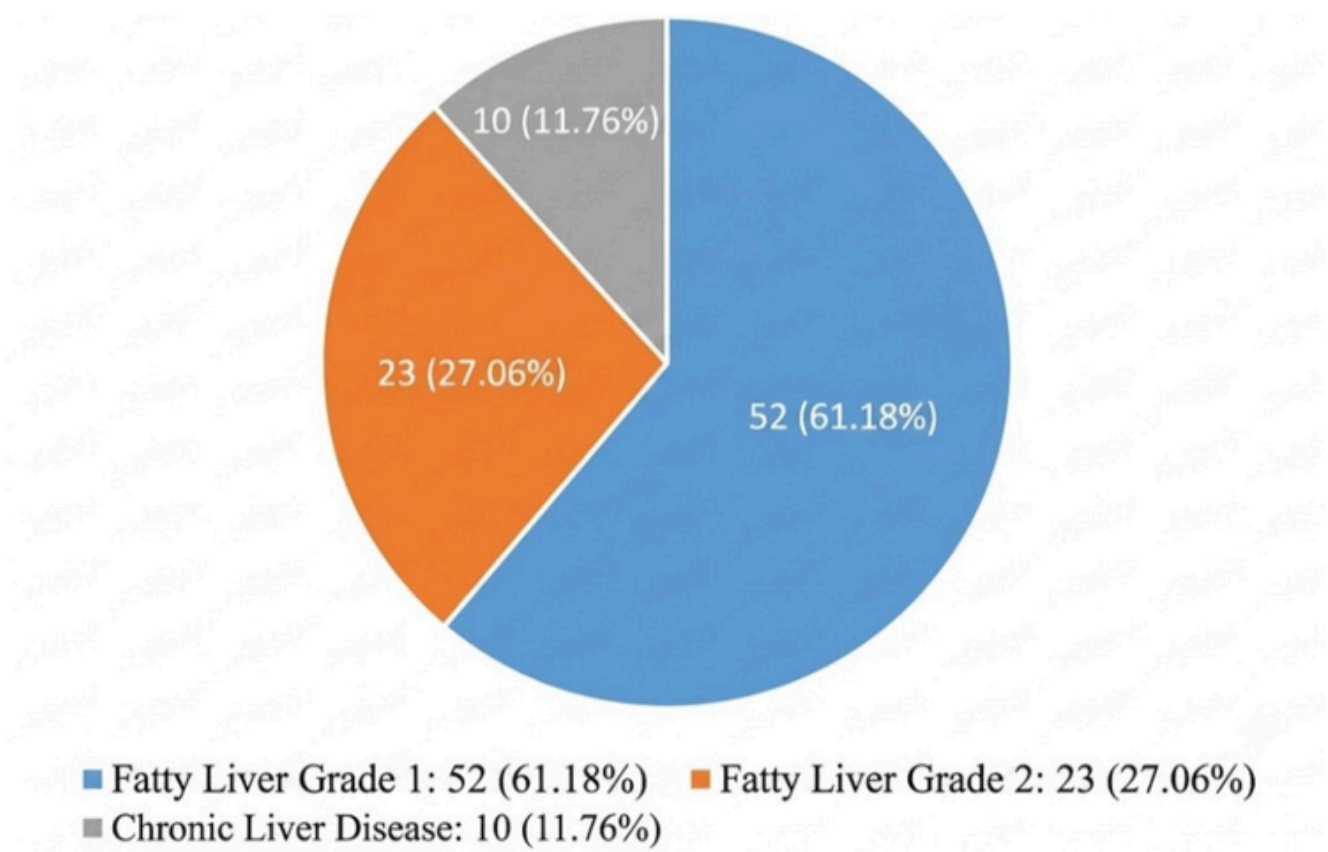


Figure 1

Distribution based on ultrasonographic diagnosis

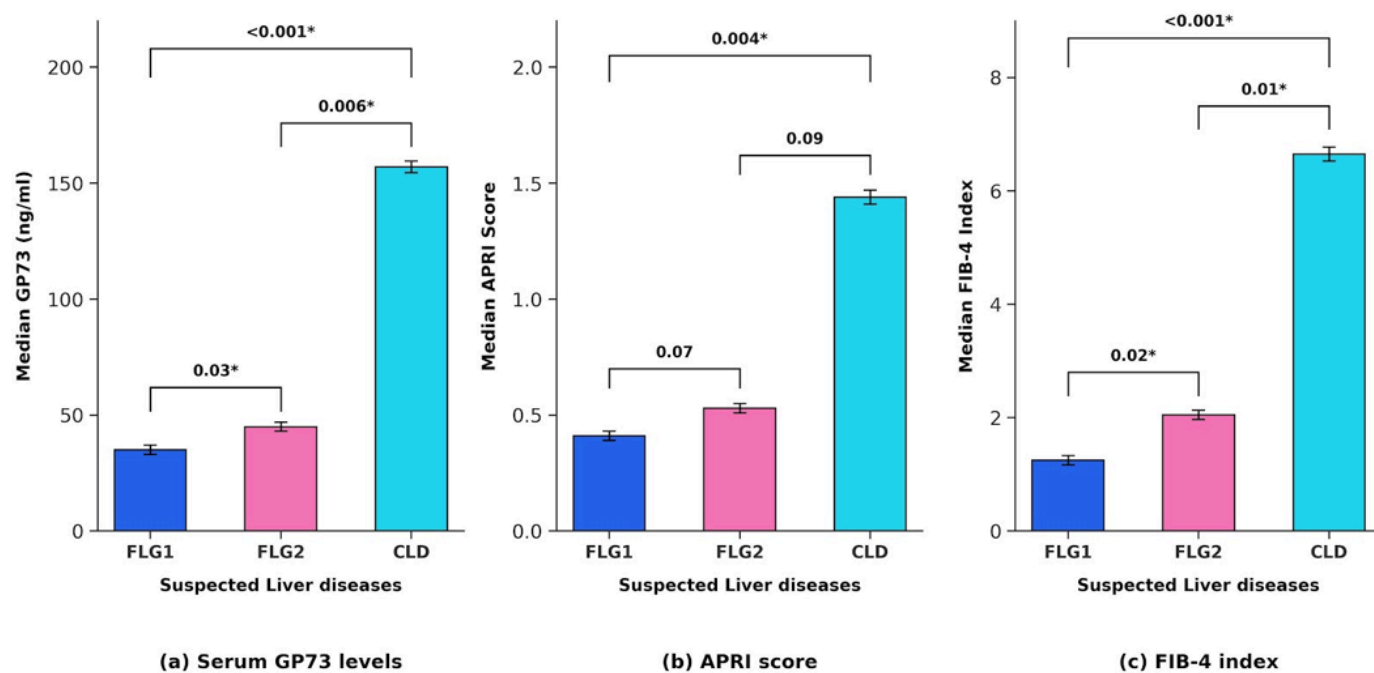


Figure 2

Pairwise comparisons of Serum GP73 levels, APRI score, and FIB-4 index among study cohorts

*p<0.05

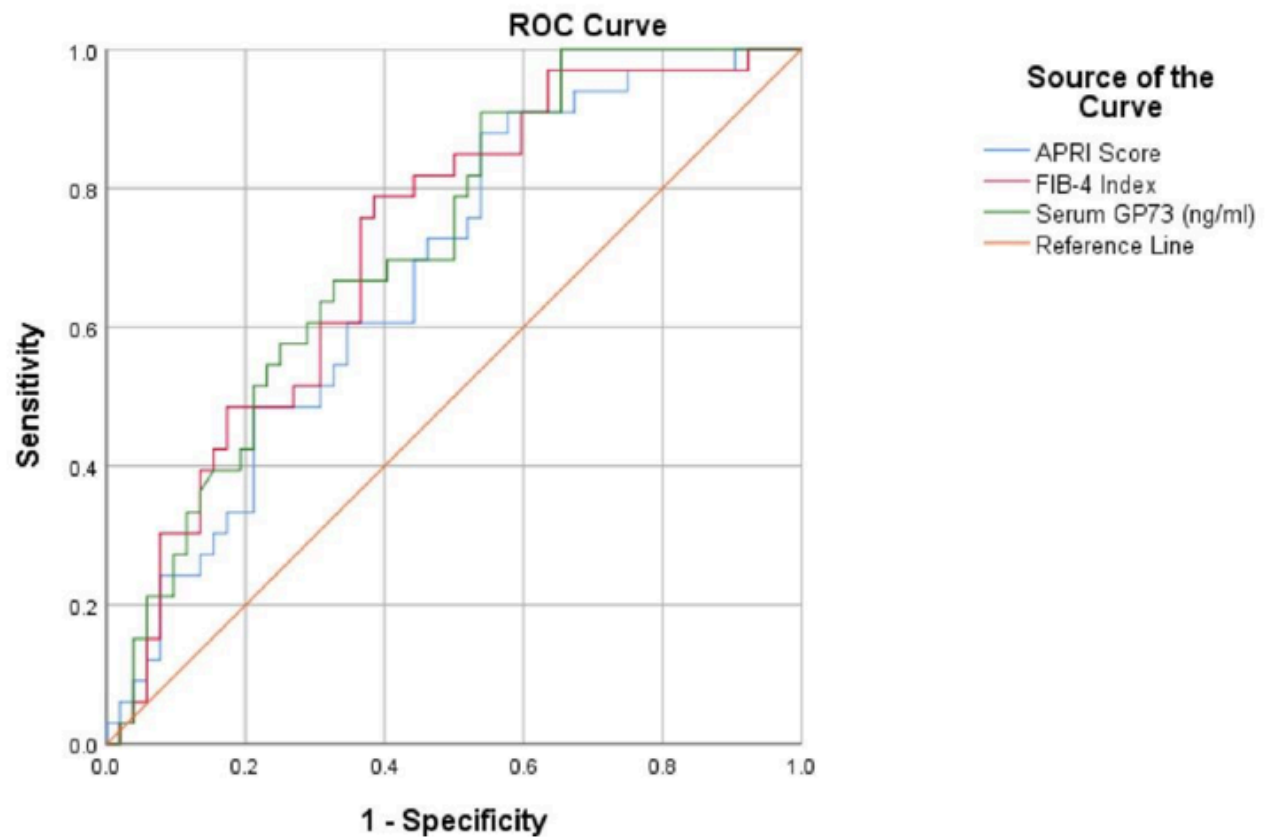


Figure 3

ROC Curve analysis of serum GP73, APRI Score, and FIB-4 Index for the diagnosis of liver disease.