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Evaluating the Relationship Between HARI and the Severity of Hepatic Steatosis in Patients with Non-Alcoholic Fatty Liver Disease (NAFLD): A Case-Control Study

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Abstract: ***Background: Non-alcoholic fatty liver disease (NAFLD) is a growing global health concern, ranging from simple hepatic steatosis to non-alcoholic steatohepatitis (NASH) and fibrosis. Early detection of disease severity is crucial for patient management. Hepatic artery resistive index (HARI), measured via Doppler ultrasound, may reflect underlying changes in hepatic hemodynamics associated with fat infiltration. Prior evidence suggests an inverse relationship between HARI and liver fat accumulation, prompting further investigation into its potential as a non-invasive biomarker. Objective: To evaluate the relationship between HARI values and the severity of hepatic steatosis in NAFLD patients, and to determine whether HARI can be used as a diagnostic parameter for assessing steatosis severity in clinical settings. Methods: A case-control study was conducted involving 50 adult participants (25 NAFLD patients and 25 controls) at J.J.M Medical College, Davangere. NAFLD was diagnosed using conventional B-mode ultrasound, and hepatic steatosis was graded by severity. HARI was measured using Doppler ultrasound of the hepatic artery. Participants with alcohol use disorder, viral hepatitis, or autoimmune liver disease were excluded. Statistical analysis was performed using independent samples t-test to compare Doppler parameters between cases and controls. Results: HARI was significantly lower in NAFLD patients compared to controls ($p < 0.0001$), particularly in those with moderate to severe steatosis. No significant difference was observed in HARI between patients with mild steatosis and controls. Additionally, there was no significant difference in hepatic artery PSV and EDV values across groups. These findings indicate a strong inverse correlation between HARI and steatosis severity.***

Keywords: Non-Alcoholic Fatty Liver Disease (NAFLD) Hepatic Artery Resistive Index (HARI), Hepatic Steatosis

Abbreviations

HARI	hepatic artery resistive index
RI	Resistive Index
PSV	Peak Systolic Velocity
EDV	End Diastolic Velocity

1. Introduction

Non-alcoholic fatty liver disease (NAFLD) is characterized by fat accumulation in the liver, ranging from simple steatosis to non-alcoholic steatohepatitis (NASH). Accurate assessment of steatosis severity is crucial for management.

The hepatic artery resistive index (HARI), a non-invasive ultrasound Doppler measurement, may reflect changes in hepatic blood flow dynamics.

Previous studies suggest HARI decreases with increasing liver fat accumulation.

This study investigates the relationship between HARI values and the severity of hepatic steatosis in NAFLD patients.

2. Materials and Methods

Study Design: Case-control study with sample size of 50.
Cases: 25 patients diagnosed with hepatic steatosis based on imaging (e.g., ultrasound).
Controls: 25 matched individuals without hepatic steatosis.

Inclusion Criteria: Adults aged 18-75, diagnosed with hepatic steatosis confirmed by imaging.

Exclusion Criteria: Alcohol use disorder, viral hepatitis, autoimmune liver diseases.
Ethical committee clearance was obtained from institution and informed consent was taken prior to the study.

Sample technique: Cohrans equation used for above study.
No other variables observed during study

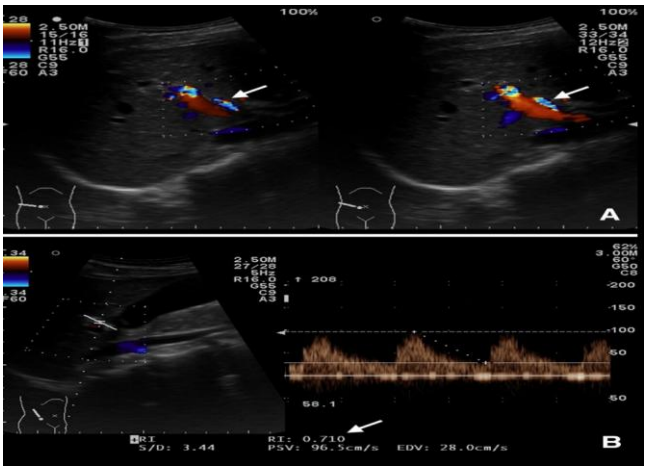
Data Collection:

Imaging: Liver ultrasound to assess steatosis severity (e.g.severity of steatosis).

The grading of HS depending on the sonographic features [23].

Steatosis Grade	Sonographic Features
0 Normal liver	Normal liver echogenicity
1 Mild	Mildly hyperechoic liver parencyhma, no vessel blurring, normal diaphragm visualization
2 Moderate	Moderately hyperechoic liver parenchyma, blurred liver vessels, impaired visualization of diaphragm
3 Severe	Remarkably hyperechoic liver parenchyma, inadequate visualization of posterior portion of the right lobe, liver vessels and diaphragm

HARI Measurement: Conducted using Doppler ultrasound of the hepatic artery.



Statistical analysis:
In this case-control study, we evaluated the relationship between Hepatic Arterial Resistance Index (HARI) and the severity of hepatic steatosis in 50 participants (25 NAFLD patients and 25 controls).

B-mode and Doppler ultrasound parameters were compared between the groups, and statistical analysis was performed using an independent samples t-test.

The results revealed that HARI was significantly lower in NAFLD patients compared to controls ($p < 0.0001$), indicating a strong association between reduced HARI and the presence of hepatic steatosis.

This finding highlights the potential of HARI as a marker for assessing liver dysfunction in NAFLD.

3. Results

HARI of NAFLD patients with different NAFLD vs controls: There was a significant difference between HARI of NAFLD patients with different NAFLD fibrosis scores vs HARI of controls, with significant differences between mS and SS, and MS and SS (p\0.0001).

HARI of NAFLD patients with different severity of diffuse fatty liver disease vs controls: There was no significant difference between hepatic artery PSV and EDV of NAFLD patients vs controls. However, HARI was significantly lower in NAFLD patients (MS and SS groups) than controls (p\0.0001). Furthermore, a significant difference was also found between the groups of severity. There was no significant difference between HARI of mS NAFLD patients vs controls.

Comparative Analysis of HARI in NAFLD Patients and Controls

Parameter	NAFLD Patients: n=25	Controls n=25	Statistical Test	P value
HARI	Lower Mean HARI	Higher Mean HARI	Independent Sample t-test	<0.001
B mode Ultrasound	Compared	Compared	Independent Sample t-test	NS*
Doppler Ultrasound: PSV EDV	Compared	Compared	Independent Sample t-test	NS*

Hepatic Artery Parameters	mS (n= 8)	MS (n= 11)	SS (n= 6)	Controls (n= 25)	P*
PSV (cm/s)	66.39 ± 33.39	68.32 ± 23.86	55.23 ± 33.48	58.15 ± 24.85	NS
EDV (cm/s)	14.08 ± 6.91	18.51 ± 8.04	19.07 ± 12.71	11.23 ± 6.84	NS
RI	0.81 ± 0.06	0.73 ± 0.04	0.61 ± 0.10	0.85 ± 0.01	<0.0001

mS: Mild steatosis MS: Moderate steatosis SS: severe steatosis

4. Discussion

In this study, we found a significant inverse correlation between HARI and severity of diffuse fatty liver disease in NAFLD patients, with a significant decrease in HARI as severity of fatty disease increases.

These results substantially confirm the data published previously. While the conventional US is sensitive and specific in the diagnosis of fatty liver disease, it cannot distinguish, with traditional parameters, patients at high risk of fibrosis. Data of previous studies suggest that clues of steatohepatitis in NAFLD patients can be an increase in portal vein diameter, reduction of portal vein velocity, large splenic area, and an increase in RI of splenic artery.

In our baseline, similar characteristics were found in NAFLD patients with severe fatty liver disease.

The recent development of novel techniques, such as elastography, has led to great advances in the assessment of liver fibrosis, but these methods are currently not available everywhere, are expensive, and need additional US equipment

However, some limitations affect our study.

First, sample size (both patients and controls) was limited; therefore, these results should be considered as preliminary and should be validated by large studies before considering them in clinical practice.

Second, hepatic artery is a vessel of difficult US approach and is not always well visualized, in particular in obese patient with severe fatty liver disease, resulting often in not diriment examinations or in false positive reduction of HARI.

5. Conclusions

This case-control study established a statistically significant inverse relationship between hepatic artery resistive index (HARI) and the severity of hepatic steatosis in patients with non-alcoholic fatty liver disease (NAFLD).

As the severity of steatosis increased—particularly in moderate to severe cases—HARI values progressively declined, while patients with mild steatosis showed no significant difference from controls. These findings indicate that HARI, a non-invasive Doppler ultrasound parameter, can reflect alterations in hepatic hemodynamics associated with fat infiltration, making it a promising adjunct tool for early detection and grading of NAFLD.

Although conventional B-mode ultrasound effectively identifies fatty infiltration, it lacks specificity in evaluating fibrosis or predicting progression to non-alcoholic steatohepatitis (NASH). HARI may bridge this gap by offering dynamic physiological insights. However, challenges such as the technical difficulty of hepatic artery visualization, particularly in obese patients, and the limited sample size of the study must be addressed.

In conclusion, HARI demonstrates potential as a cost-effective, widely accessible, and non-invasive biomarker for assessing hepatic steatosis severity. Its incorporation into routine ultrasound protocols may enhance risk stratification and guide timely intervention in NAFLD patients, especially in resource-limited settings.

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