RESEARCH ARTICLE

Navigating non-alcoholic fatty liver disease (NAFLD): understanding the correlation between hepatic vein and portal vein doppler indices and fatty liver grades

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Abstract

Objective: To determine the association of fatty liver ultrasound grade with hepatic venous waveform, hepatic vein damping index and portal vein pulsatility index.

Method: The cross-sectional, prospective, analytical study was conducted at the Radiology Department of the Pakistan Kidney and Liver Institute and Research Centre, Lahore, Pakistan, from January 1 to June 30, 2023, and comprised patients who underwent ultrasound scans with a low-frequency curvilinear transducer. Data was collected on fatty liver grade, middle hepatic vein waveform, middle hepatic vein damping index and portal vein pulsatility index. The relationship of fatty liver grades with hepatic vein waveform, hepatic vein damping index and portal vein pulsatility index. Data was analysed using SPSS 27.

Results: Of the 45 patients, 26(57.88%) were females and 19(42.22%) were males. The overall mean age was 43.16±11.55 years. Among the patients, 36(80%) had a grade-1 fatty liver, while 9(20%) had a grade-2 fatty liver. Mean middle hepatic vein damping index between grade 1 and grade 2 fatty liver patients was significant ($p<0.001$). The mean portal vein pulsatility index of grade 1 fatty liver patients was significantly different from grade 2 patients ($p<0.001$). Fatty liver sonological grade had a moderate and direct relationship with middle hepatic vein damping index ($r=0.652$), but an inverse relationship was observed between fatty liver sonological grade and portal vein pulsatility index ($r=-0.427$).

Conclusion: Significant correlations existed between ultrasound fatty liver grade and hepatic vein waveforms, hepatic vein damping index and portal vein pulsatility index.

Key Words: Non-alcoholic fatty liver disease, Hepatic veins, Portal vein, Ultrasound.

(JPMA 75: 1873; 2025) **DOI: https://doi.org/10.47391/JPMA.25-20988**

Introduction

Non-alcoholic fatty liver disease (NAFLD) is a worldwide prevalent cause of chronic liver disease (CLD).1 In a recent meta-analysis, its incidence was estimated to be 46.9 cases per 1,000 person-years.[2] In NAFLD, there is excessive steatosis in hepatocytes, associated with insulin resistance (IR), and characterised by fat accumulation in >5% hepatocytes.[3] Most patients with NAFLD are asymptomatic, and diagnosed on routine examinations, presenting only with mildly elevated levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT).[4] However, NAFLD can advance to non-alcoholic steatohepatitis (NASH), later being complicated by cirrhosis, hepatocellular carcinoma (HCC), liver transplantation, and mortality.[5]

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Submission complete: 18-06-2024 **First Revision received:** 10-09-2024

Acceptance: 30-08-2025 **Last Revision received:** 29-08-2025

Hepatic biopsy has been the benchmark for the diagnosing and calculation of hepatic fat content, and to distinguish NAFLD from NASH. However, due to its invasive nature and associated complications, it is reserved for high-risk patients' follow-up and to quantify hepatic fibrosis.[6] Ultrasound (US) is a cost-effective, readily available tool and is most frequently employed initially to diagnose and grade fatty liver disease (FLD).[7,8] The greyscale US has a sensitivity of 53-76% and a specificity of 76-93% for the diagnosis of hepatic steatosis.[9]

Recent research suggests that liver parenchymal diseases, including FLD, cirrhosis and fibrosing diseases, directly affect hepatic vascular haemodynamics hinting at vascular compliance. However, how much of this Doppler index alteration can be attributed to hepatic parenchymal fat accumulation is still debatable.[10, 11]

NAFLD is a common problem in Pakistan with a prevalence of 14% and is known to progress to NASH, cirrhosis and ultimately malignancy.[12] Hence, it is crucial to investigate the impact of NAFLD on Doppler US flow patterns. The current study was planned to explore the

association between fatty liver grades and hepatic venous as well as portal venous Doppler indices.

Patients and Methods

The cross-sectional, prospective, analytical study was conducted at the Radiology Department of the Pakistan Kidney and Liver Institute and Research Centre, Lahore, Pakistan, from January 1 to June 30, 2023, following approval from the institutional ethics review board. The sample was raised using consecutive sampling technique. The sample size was determined using the World Health Organisation (WHO) calculator[13], based on the formula for estimating a population proportion with specified absolute precision. Parameters included 95% confidence interval (CI), anticipated population proportion (P) 0.10, and absolute precision (d) 0.09. NAFLD prevalence was taken as 13.5%.[14] The study included patients of all ages and genders diagnosed with fatty liver on US who visited the radiology department for an abdominal ultrasound. Patients unable to hold their breath for Doppler indices recording were excluded, and so were those with known cardiac disease, and individuals with any other concurrent liver conditions.

US scans were performed (GE Logiq P7 and GE Logiq S8 Class I, 100-240 V~, 50/60 HZ, 500-5000VA GE Ultrasound Korea, Ltd.) using a low-frequency curvilinear transducer (3.5-6.5MHz). Following informed consent from each patient, data on fatty liver grade (1-3), middle hepatic vein (MHV) waveform, middle hepatic vein damping index (MHVDI), and portal vein pulsatility index (PVPI) were recorded on a standardised proforma. The findings were independently reviewed by a second radiologist/sonologist to mitigate bias.

Data was analysed using SPSS 27. Categorical data was presented as frequencies and percentages, while numerical data was presented as mean ± standard deviation. Shapiro-Wilk test was used to check data normality, and age (p=0.970), MHVDI (p=0.423) and PVPI (p=0.689) data was found to be normally distributed. Person correlation was used for numerical variables, and Kendall's tau correlation was used, due to repeated grade scores, to assess the relationship of fatty liver grades with MHV waveform, MHVDI and PVPI. Chi-square test was applied to determine the association between categorical data waveform patterns and fatty liver grades. Student's t test was used to determine the mean difference between MHVDI and PVPI with regard to FLSG. P≤0.05 was considered significant.

Results

Of the 45 patients, 26(57.88%) were females and 19(42.22%) were males. The overall mean age was 43.16±11.55 years (range:16-69 years). There were 12(26.7%) patients aged 16-35 years and 33(73.3%) were aged 36-69 years. Age was not associated with gender, MHV waveform and FLSG (p>0.05) (Table 1).

None of the Doppler US scans showed a monophasic waveform. Among the patients, 36(80%) had a grade-1 fatty liver, all of whom exhibited a triphasic MHV waveform. The remaining 9(20%) patients had a grade-2 fatty liver, and, of them, 7(77.8%) had a biphasic MHV

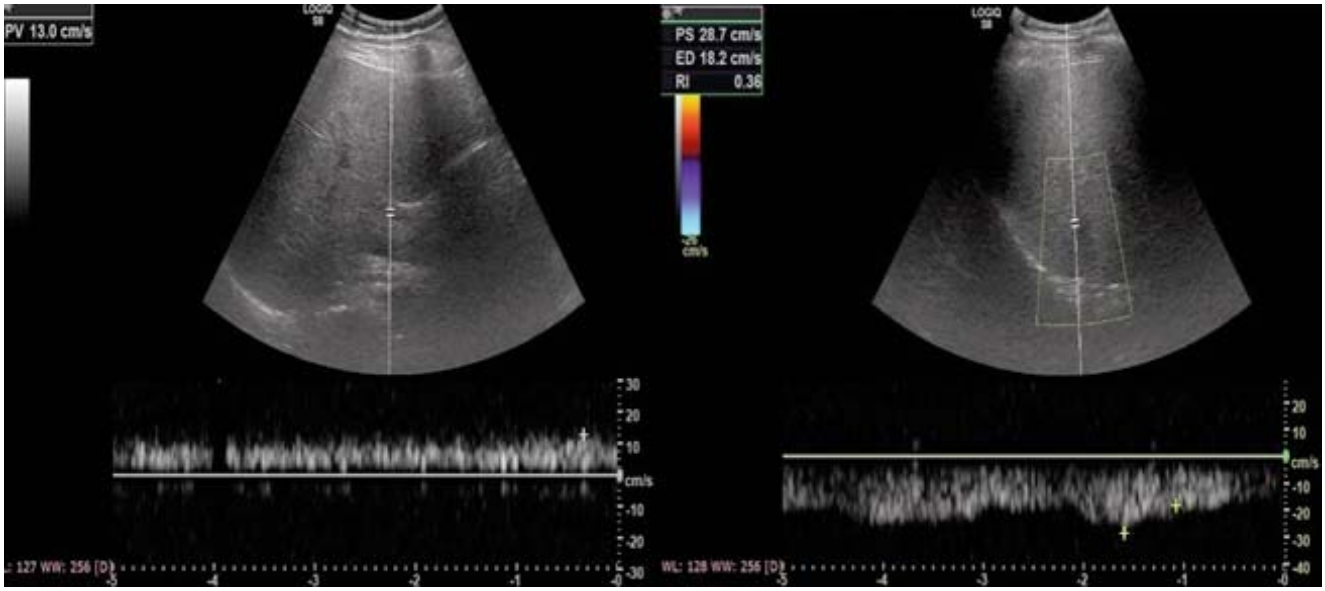

Figure-1: Doppler imaging of a patient with grade 1 fatty liver (top). The portal vein spectrum (top right) is pulsatile. The hepatic vein spectrum (top left) is triphasic.
Doppler imaging of a patient with grade 2 fatty liver (bottom). The portal vein spectrum (bottom right) is non-pulsatile. The hepatic vein spectrum (bottom left) is biphasic.

Table-1: Distribution of fatty liver sonological grade and MHV waveform according to age groups

Studied Factors	Categories	Age Group 16-35 years n=12	Age Group 36 -69 years n=26
Gender			
	Male	7(36.8%)	12(63.2%)
	Female	5(19.2%)	21(80.8%)
MHV wave form	Triphasic	10(27.0%)	27(73.0%)
	Biphasic	2(25.0%)	6(75.0%)
Fatty liver sonological grade (FLSG)			
	Grade I	10(27.0%)	27(73.0%)
	Grade II	2(25.0%)	6(75.0%)

MHV: Middle hepatic vein.

waveform, and 2(22.2%) had a triphasic waveform (Figure 1).

Mean MHVDI of grade-1 fatty liver patients was 0.47±0.15 (range: 0.15-0.67) and among grade-2 fatty liver patients it was 0.76±0.08 (range: 0.10-0.33) (p<0.001).

Mean PVPI of grade-1 fatty liver patients was 0.39±0.10 (range: 13.95-58.62) and that of grade-2 fatty liver patients was 0.25±0.08 (range: 0.64-0.85) (p<0.001) (Figure 2).

There was a moderate and direct relationship between FLSG) and MHVDI (r=0.562), a strong and direct relationship between FLSG and MHV waveform (r=0.858), and an inverse relationship between FLSG and PVPI (r=-0.427) (Table 2).

Discussion

The portal venous flow in the normal population is continuous and pulsatile and its pulsatility index (PI) in healthy adults is 0.48.[15, 16] Gallix et al. also concluded that PI is inversely related to the body mass of an individual. The hepatic veins on the other hand typically exhibit a triphasic pattern characterised by cardiac motion and respiratory fluctuations, since a healthy liver can adjust to these changes. However, in a stiff and diseased liver, as in inflammatory liver diseases, NAFLD, hepatic mass lesions and ascites, this waveform is altered and dampened.[17]

The results of the current study showed that the MHV waveform deranged from triphasic to biphasic as the fatty liver grade increased. This is in keeping with the results of

Table-2: Correlation of fatty liver grade with MHV vein waveform, MHVDI and PVPI.

Correlation Coefficient	MHV waveform	PV pulsatility index	MHV damping index
Fatty liver sonological grade	0.858**	-0.427**	0.562**
MHV waveform		-0.420**	0.518**
PV pulsatility index			-0.424**

MHV: Middle hepatic vein, DI: Damoing index, PVPI: Portal vein pulsatility index. Kendall's tau_b, **. Correlation is significant at the 0.01 level (2-tailed).

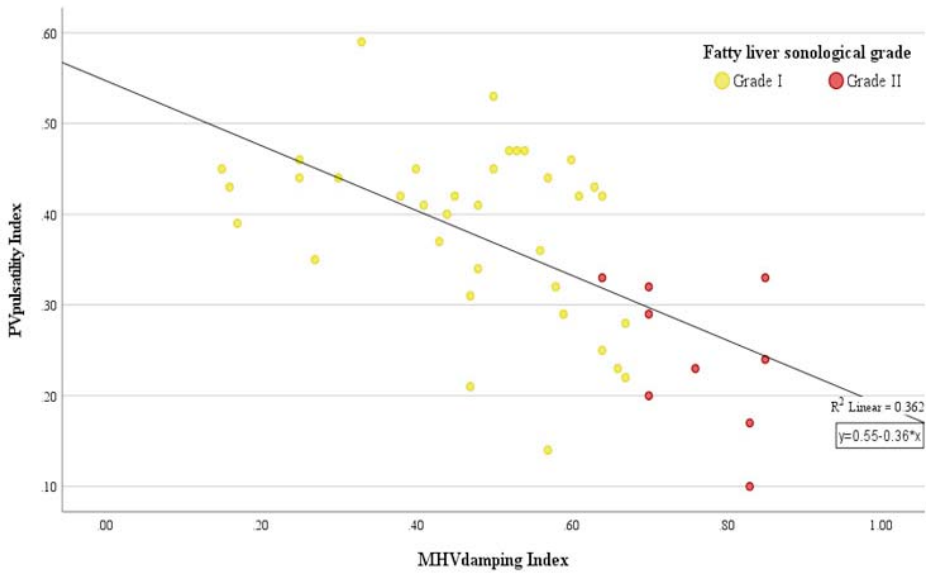

Figure-2: Scatter plot of portal vein pulsatility index (PVPI) and middle hepatic vein damping index (MHVDI) segregated according to fatty liver ultrasound grade (FLSG).

Botrous et al. who[18] reported that the waveform was monophasic or biphasic in 60% NAFLD patients. However, they did not study the relation of this derangement with the fatty liver US grade, which the current study did.

To our knowledge, the hepatic vein DI has not been studied in patients with NAFLD. However, some studies have analysed its significance in other diffuse liver disease. Antil et al. evaluated hepatic vein DI in patients with cirrhosis and discovered a positive correlation between DI and Child score ($r=0.614$, $p<0.05$).[19] They also suggested that derangement in the hepatic vein waveform and a DI >0.6 were predictors of severe liver disease and portal hypertension. Similarly, another study concluded that a DI cut-off value of 0.6 had a sensitivity of 75.9% and a specificity of 81.8% for predicting severe portal hypertension.[20] More recently, Abdelmonem et al. studied the relationship between hepatic vein DI and Child score in patients with liver cirrhosis, and concluded that 62.5% patients had a DI >0.6.[21] The current results showed a strong positive correlation between DI and fatty liver US grade ($r=0.675$, $p<0.001$) which was similar to the above-mentioned studies.

Recently, Hamed et al. stratified patients with NAFLD into low-risk and high-risk groups, and studied the PVPI in both of these groups in combination with other clinical parameters.[22] They concluded that PVPI was a valuable biomarker in conjunction with other established clinical predictors for the assessment of NAFLD. Their values of PVPI for low-risk and high-risk groups were 0.32±1.25 and 0.20±2.61, respectively. These are close to the current results where the PVPI ranged 0.1-0.59, with a mean of 0.35±0.11. However, Hamed et al. did not study the PVPI correlation with fatty liver US grade which the current study did. Baikpour et al. did a study similar to Hamed et al. and divided NAFLD patients into high-risk and low-risk groups showing significant differences in PVPI values (0.19 vs 0.32, $p<0.001$).[23]

Lee et al. categorised NAFLD patients into fibrotic and non-fibrotic groups based on US elastography findings, and explored the PVPI and mean portal vein diameter in these patients.[24] They observed significant differences between PVPI values of fibrotic and non-fibrotic groups (0.27 vs 0.34, $p<0.001$). These results were in keeping with the current findings regarding PVPI.

The current study has limitations as it did not include a control group without FLD which would have made it more comprehensive.

Conclusion

There were significant correlations between US fatty liver grade and hepatic vein waveforms, hepatic vein DI, and PVPI in patients with NAFLD. This highlighted the potential utility of Doppler US parameters in assessing and grading FLD, providing valuable non-invasive diagnostic data.

Acknowledgement: We are grateful to Huma Hussain for editorial assistance.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

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AUTHOR'S CONTRIBUTION:
MSR: Concept, design and data acquisition.
SZ: Data acquisition, interpretation and intellectual input to the content.
FS: Data acquisition, analysis and drafting.
BB: Data acquisition and interpretation.
KK: Critical analysis.