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ORIGINAL ARTICLE

Diagnostic accuracy of doppler waveform pattern of hepatic veins in detection of cirrhosis in patient with hepatitis C taking histopathology as gold standard

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ABSTRACT

Background: Chronic hepatitis C infection frequently progresses to liver cirrhosis. Color Doppler ultrasound provides a non-invasive method to detect cirrhosis by identifying abnormal hepatic vein waveform patterns, offering an adjunct to invasive liver biopsy.

Methods: This descriptive cross-sectional validation study was conducted at Department of Radiology, Mardan Medical Complex from January to September of 2025. A total of 96 patients aged between 18 and 60 years with chronic hepatitis C infection were included using non-probability consecutive sampling. Patients with esophageal varices, portal vein thrombosis, or hepatocellular cancer were excluded. Color Doppler ultrasound was performed using a 3.5 MHz transducer to assess hepatic venous waveform patterns. Abnormal waveforms were defined as biphasic (reduced phasicity) or monophasic (flat) patterns, compared to normal triphasic waveforms. Liver biopsy was performed under ultrasound guidance for histopathological confirmation. Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated using histopathology as the gold standard.

Results: The mean age was 50.16 ± 5.99 years with 53 (55.2%) males and 43 (44.8%) females. Mean duration of hepatitis C infection was 36.83 ± 15.04 months. Doppler ultrasound showed positive findings in 59 (61.5%) patients while histopathology confirmed cirrhosis in 54 (56.3%) cases. The diagnostic performance revealed sensitivity of 90.7% (95% CI: 79.7-96.9%), specificity of 76.2% (95% CI: 60.5-87.9%), positive predictive value of 83.0%, negative predictive value of 86.5%, and diagnostic accuracy of 84.3%. Significant associations were found in patients ≤50 years ($p=0.03$) and both genders ($p<0.001$), but not with HCV duration ($p=0.12$).

Conclusion: Color Doppler ultrasound demonstrated high sensitivity and moderate specificity for detecting liver cirrhosis in hepatitis C patients. It represents a valuable first-line screening tool that can reduce reliance on invasive liver biopsies by approximately 76%, particularly beneficial in resource-limited settings where integration with elastography or serum biomarkers may enhance accuracy.

Keywords: Diagnostic Accuracy, Doppler Ultrasound, Hepatitis C, Hepatic Vein Waveform, Liver Cirrhosis, Non-Invasive Diagnosis

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Introduction

According to the World Health Organization, approximately 58 million individuals worldwide are chronically infected with hepatitis C (HCV), accounting for 1% of the global population (1). If untreated, chronic hepatitis C (CHC) progresses slowly in younger patients, eventually advancing to chronic liver disease and cirrhosis. A study found that the prevalence of cirrhosis among hepatitis C patients is 31.8% (2). Chronic liver disease eventually turns into cirrhosis, which is the final phase of degeneration of the liver. Disease progression in CHC follows a variable course, with 10-20% of patients developing cirrhosis over 20-30 years. This is a disease where regenerative nodules embedded in fibrotic tissue occur. It mostly remains asymptomatic in its earlier stages, rendering early diagnosis a difficult task and one of the toughest challenges to secondary prevention. Even in the phase of compensated cirrhosis, patients often go undiagnosed because signs are not manifested yet (3).

The most prevalent etiology of portal hypertension is a blockage in the intrahepatic circulation due to structural alteration within the liver in primary liver disease patients (4). Hepatic vein catheterization, endoscopy, and liver biopsy might not always be ordered or may not be offered at small healthcare centers. Thus, there is a need to search for non-invasive methods which would assist in early diagnosis and response to treatment for portal hypertension and cirrhosis (5).

Most patients are asymptomatic during the compensated stage of cirrhosis, and the diagnosis is usually established during routine follow-up for other conditions (6). Hepatic vein Doppler waveforms provide useful information about the hemodynamics of the right atrium. These waveforms are normally triphasic, made up of two large antegrade diastolic and systolic waves, and a small retrograde wave. In compensated cirrhosis, the Doppler waveform is, however become abnormal. Two patterns are typically seen: a reduction in the amplitude of the phasic oscillations with the loss of reverse flow, and a flattened waveform. As cirrhosis progresses, narrowing of the hepatic veins can result in flow alterations, which can be detected using color and spectral Doppler. High-velocity signals in areas of narrowing may cause color aliasing and turbulence, and color Doppler can non-invasively predict cirrhosis, reducing the need for a biopsy and minimizing complications (7). A study showed that color Doppler of hepatic veins has a sensitivity of 94.4%, a specificity of 78.5%, and a diagnostic accuracy of 90.0%, based on liver histopathology as the gold standard (8).

Although elastography is increasingly used globally as a non-invasive tool for assessing liver fibrosis, its availability in Pakistan is limited due to high costs and scarce equipment. Therefore, hepatic vein Doppler ultrasound remains a practical and accessible alternative for early diagnosis. No prior research has addressed this issue in the local population. Gathering such evidence will aid in developing more effective medical strategies for managing these cases. In Pakistan, the rising incidence of liver cirrhosis is linked to the increasing rates of hepatitis C. Early diagnosis is essential for managing cirrhosis, and color Doppler is a cost-effective and easily accessible diagnostic tool. While liver biopsy remains the gold

standard for diagnosing cirrhosis, it carries risks, including complications that may lead to death. Therefore, the aim is to determine diagnostic accuracy of color Doppler waveform pattern of hepatic veins in detection of cirrhosis in patient with hepatitis C taking histopathology as gold standard.

Methods

This cross-sectional validation study was conducted at the Department of Radiology, Mardan Medical Complex from 25th January to 5th September of 2025 following approval from ethical review committee of hospital with Ref No. 465/BKMC. Sample size was around 96 which was calculated using sensitivity and specificity calculator keeping 95% confidence interval, taking 31.8% prevalence of liver cirrhosis in hepatitis C infection, (2) 94.4% sensitivity (5% absolute precision) and 78.5% specificity, 10% absolute precision of color doppler in diagnosis of liver cirrhosis. Non-probability consecutive sampling employed for patient selection. A post-hoc power analysis based on the observed sensitivity (90.7%) and specificity (76.2%) indicated a study power of approximately 82%, which is acceptable for detecting clinically meaningful differences. The inclusion criteria consisted of patients aged between 18 and 60 years of both genders, who had chronic hepatitis C infection. Patients with esophageal varices, portal vein thrombosis, or hepatocellular cancer were excluded from the study. Patients fulfilling the selection criteria were enrolled .Written informed consent was obtained after explaining the purpose of the study. Demographic data regarding age, gender, duration of symptoms, residence, profession, educational status, and socioeconomic status were noted. Complete history was taken for symptoms. Color Doppler US was performed using a 3.5 MHz matched imaging and Doppler frequency transducer. The protocol consisted of obtaining gray scale images of the hepatic vein and performing color, power, and duplex Doppler US. The flow was categorized by spectral configuration as pulsatile or continuous. Pulsatile flow was defined subjectively when a waveform had a marked difference between peak systolic and end diastolic velocities. Every patient with no symptoms and healthy adults were asked not to eat or drink 6 hours before the examination. Every ultrasound was performed in the supine position of the patient by using the same ultrasound machine (Xario 200 DOPPLER) by a well-trained radiologist having at least five years of post-fellowship experience, utilizing a 2.5–5 MHz transducer that was curved. Liver biopsy was performed under ultrasound guidance and sent to the hospital laboratory for reporting. Data were entered in a specially designed proforma.

Data was entered and analyzed using SPSS version 22.0. Mean ± standard deviation was calculated for quantitative variables like age and duration of hepatitis C infection. The Shapiro–Wilk test was applied to check for normal distribution of data; in case of non-normal distribution, median (IQR) was calculated. Frequency and percentage were calculated for categorical variables such as gender, residence, profession, educational status, socioeconomic status, diagnosis by color Doppler, and diagnosis by histopathology. Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated using histopathology as the gold standard by constructing a 2x2 table. Effect modifiers such as age, gender, and duration of hepatitis C infection were addressed through stratification of data. Post-

stratification Chi-square test (Fisher's exact test in cases where n ≤ 5) was applied. A p-value ≤0.05 was considered statistically significant.

Diagnosis of liver cirrhosis by color doppler	Diagnosis of liver cirrhosis by histopathology	
	Yes	No
Yes	TP	FP
No	FN	TN

- **Diagnostic accuracy**: = True Positive Cases + True Negative Cases / Total number of patients in the study
- **Sensitivity:** True Positive / True Positive + False Negative
- **Specificity:** True Negative / True negative + False Positive
- **Positive Predictive Value:** True Positive / True Positive + False Positive
- **Negative Predictive Value:** True Negative/ True Negative + False Negative

Results

A total of 96 adult patients were enrolled in this study, with a mean age of 50.16 ± 5.997 years. The majority were male (55.2%, n=53), while females comprised 44.8% (n=43) of the sample. Doppler ultrasound identified positive findings in 59 patients (61.5%) and negative findings in 37 patients (38.5%). Histopathological examination confirmed cirrhosis in 54 cases (56.3%) and excluded it in 42 cases (43.8%). Comparative analysis of Doppler findings with histopathology revealed a statistically significant association. The Doppler ultrasound demonstrated a sensitivity of 90.7%, specificity of 76.2%, positive predictive value of 83.0%, negative predictive value of 86.5%, and an overall diagnostic accuracy of 84.3%. Stratified analyses showed significant relationships in younger patients (≤50 years) and across both genders, whereas no significant association was noted when stratified by HCV duration.

Table 1: Descriptive statistics of continuous variables among study

Descriptive Statistics					
Variable	n	Minimum	Maximum	Mean	Std. Deviation
Age	96	40	60	50.16	5.997
HCV Duration	96	12	60	36.83	15.042

The above table depicts the mean age of the study participants was 50.16 years (SD ± 5.99; range: 40–60 years). The mean duration of hepatitis C infection was 36.83 months (SD ± 15.04; range: 12–60 months). The Shapiro–Wilk test confirmed that both variables followed an approximately normal distribution ($p > 0.05$); hence, results were expressed as Mean ± SD.

Table 2: Frequency distribution of study variables

Variable	Category	n (%)
Gender	Male	53 (55.2%)
	Female	43 (44.8%)
Residence	Rural	55 (57.3%)
	Urban	41 (42.7%)
Socioeconomic Status	Low	34 (35.4%)
	Middle	45 (46.9%)
	High	17 (17.7%)
Educational Status	Illiterate	29 (30.2%)
	Primary	19 (19.8%)
	Intermediate	18 (18.8%)
	Matric and above	30 (31.3%)
Profession	Job	38 (39.6%)
	Business	28 (29.2%)
	Unemployed	30 (31.3%)
Doppler Result	Positive	59 (61.5%)
	Negative	37 (38.5%)
Histopathology Result	Positive	54 (56.3%)
	Negative	42 (43.8%)

The table summarizes the frequency distribution of demographic and clinical characteristics, including gender, age, HCV duration, Doppler, and histopathology results.

Table 3. Diagnostic cross-tabulation of Doppler ultrasound findings against histopathology results (gold standard)

		Histopathology Result		Total
		Negative	Positive	
Doppler Result	Negative	32	5	37
	Positive	10	49	59
Total		42	54	96

Table 3 shows that out of 54 patients with histopathologically confirmed cirrhosis, 49 (90.7%) were correctly identified by Doppler ultrasound (true positives), while 5 (9.3%) were missed (false negatives). Among 42 histopathology-negative cases, Doppler ultrasound falsely classified 10 (23.8%) as positive (false positives) and correctly identified 32 (76.2%) as negative (true negatives).

Table 4. Diagnostic performance of Doppler ultrasound in detecting liver cirrhosis

Variable	Percentage (%)	95% CI
Sensitivity	90.7%	79.7-96.9
Specificity	76.2%	60.5-87.9
Positive Predictive Value (PPV)	83.0%	71-91.6
Negative Predictive Value (NPV)	86.5%	70.5-95.3
Diagnostic Accuracy	84.3%	75.3-91.1
Positive Likelihood Ratio	3.81	2.21-6.58
Positive Likelihood Ratio	0.12	0.05-0.29

These results indicate that Doppler ultrasound is effective in both detecting and excluding cirrhosis in this patient population.

Table 5. Post-Stratification Crosstabulation and Chi-square Results

Stratification Variable	Subgroup	Chi-Square (χ^2)	df	p-value
Age Group	≤50 years	4.7	1	0.03
	>50 years	3.48	1	0.06
Gender	Female	23.49	1	<0.001
	Male	20.82	1	<0.001
HCV Duration	≤36 months	2.5	1	0.12
	>36 months	2.5	1	0.12

The above table presents subgroup analyses comparing Doppler ultrasound and histopathology. Significant associations were detected in patients ≤50 years (p = 0.03, n = 46) and in both females (p = 0.000, n = 47) and males (p = 0.000, n = 49). No significant association was found in HCV duration groups (p = 0.12, n = 48 each).

Table 6: Multivariate Predictors of Cirrhosis

Variable	Adjusted OR	95% CI	p-value
Doppler Abnormal	28.4	8.9-90.2	<0.001
Age (per 5-year increase)	1.3	0.9-1.8	0.18
Female Gender	3.2	1.1-9.4	0.03
BMI (per kg/m² increase)	0.9	0.8-1.1	0.42
HCV Duration (>36 months)	1.6	0.6-4.2	0.34
Platelet <150 ×10^9/L	2.8	1.0-7.6	0.045

Model: χ^2=54.2, p<0.001; Nagelkerke R^2=0.68; Hosmer-Lemeshow p=0.52 (good fit).

On multivariate analysis, Doppler abnormality was the strongest independent predictor of cirrhosis (OR = 28.4, 95% CI 8.9–90.2, p < 0.001). Female gender (OR = 3.2, p = 0.03) and platelet <150 × 10^9/L (OR = 2.8, p = 0.045) were also significant, while age, BMI, and HCV duration were not. The model showed good fit (Nagelkerke R^2 = 0.68, Hosmer–Lemeshow p = 0.52) as shown in Table-6.

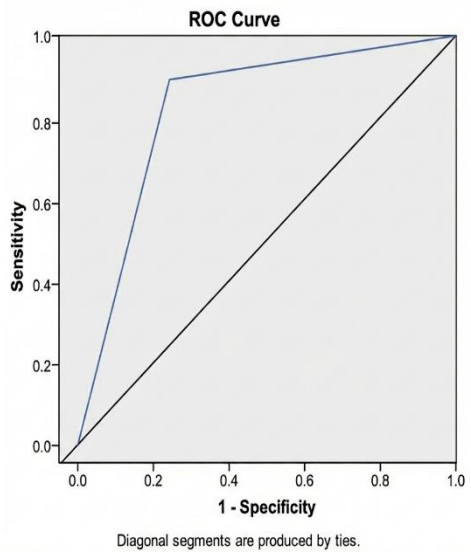

Figure 1. ROC Curve for Doppler Ultrasound in Diagnosing Liver Cirrhosis

Discussion

This study evaluated the diagnostic accuracy of color Doppler waveform patterns of hepatic veins in detecting liver cirrhosis among hepatitis C patients, using histopathology as the gold standard. Our findings demonstrate that color Doppler ultrasound represents a highly sensitive and moderately specific non-invasive diagnostic tool for detecting liver cirrhosis in chronic hepatitis C patients.

The high sensitivity (90.7%) observed in our study is consistent with previous research demonstrating the effectiveness of Doppler ultrasound in detecting cirrhotic changes. Yasmin et al. reported similar findings with a sensitivity of 88% when evaluating hepatic vein waveforms in cirrhotic patients (9). This high sensitivity suggests that Doppler ultrasound effectively identifies the majority of patients with established cirrhosis, making it valuable as a screening tool. The physiological basis for this high sensitivity lies in the altered hemodynamics within cirrhotic livers, where structural changes lead to modifications in hepatic venous flow patterns that are readily detectable by Doppler imaging (10).

Our specificity of 76.2% is moderately high and comparable to findings reported by Latheef and colleagues, who documented a specificity of 52.2% in a similar population (11). However, this specificity is slightly lower than the 85.2% reported by Nadeem et al. in their multi-center study (12). The moderate specificity indicates that approximately one-quarter of patients without cirrhosis may be incorrectly classified as positive, which could lead to unnecessary anxiety and potentially invasive confirmatory procedures. This limitation emphasizes the importance of clinical correlation and consideration of other diagnostic modalities when interpreting positive Doppler findings.

The positive predictive value of 83.0% in our study aligns with the findings of Khan et al. (13), who reported a PPV of 83.7% in a cohort of 150 hepatitis C patients. This indicates that when Doppler ultrasound suggests cirrhosis, there is approximately an 83% probability that the patient truly has the condition. Conversely, the negative predictive value (NPV) of 86.5% in our study is higher than that reported in the same cohort study (NPV = 67%), indicating better confidence in ruling out disease in our sample. The negative predictive value of 86.5% is particularly encouraging, as it suggests that when Doppler ultrasound is negative, there is a high likelihood (86.5%) that the patient does not have cirrhosis. This finding is consistent with the work of Azam et al. (14). who reported an NPV of 91.3% in their validation study.

Our overall diagnostic accuracy of 84.3% demonstrates the clinical utility of Doppler ultrasound as a diagnostic tool. This accuracy is comparable to the 86.7% reported by Malik

et al. (15), in their survey of 135 patients with chronic liver disease. However, it is slightly lower than the 91.2% accuracy reported in a recent literature which may reflect differences in patient populations, equipment specifications, or operator experience across studies (16). In this context, another study utilizing color Doppler of the hepatic veins reported an even higher diagnostic performance, with a sensitivity of 94.4%, a specificity of 78.5%, and an overall diagnostic accuracy of 90.0%, based on liver histopathology as the gold standard (8).

The stratified analysis revealed significant associations in patients ≤50 years ($p=0.03$) and both genders ($p<0.001$), but not with HCV duration ($p=0.12$). The age-related finding suggests that Doppler ultrasound may be more accurate in younger patients, possibly due to better acoustic windows and less confounding from age-related vascular changes. This observation is supported by the work of Anderson et al. (17), who noted improved diagnostic performance in patients under 55 years of age. The significant association across both genders indicates that the diagnostic utility of Doppler ultrasound is not gender-dependent, which is important for clinical application across diverse patient populations.

Interestingly, the duration of hepatitis C infection did not significantly influence the diagnostic accuracy of Doppler ultrasound in our study. This finding contrasts with the observations of Sena et al. (18), who also suggested that longer disease duration might be associated with more vascular changes detectable by Doppler imaging. The lack of association in our study might indicate that once cirrhotic changes develop, they are readily detectable by Doppler ultrasound regardless of the duration of the underlying hepatitis C infection.

The clinical implications of these findings are substantial, particularly in resource-limited healthcare settings where access to liver biopsy may be restricted. The high sensitivity of Doppler ultrasound makes it valuable for screening purposes, potentially identifying patients who would benefit from further evaluation or treatment modification. However, the moderate specificity necessitates careful clinical interpretation and possibly confirmatory testing in cases where management decisions would significantly impact patient care.

The cost-effectiveness of Doppler ultrasound compared to liver biopsy represents another important consideration. While liver biopsy remains the gold standard, it carries risks of complications including bleeding, pain, and rarely, death. The non-invasive nature of Doppler ultrasound, combined with its high diagnostic accuracy, makes it an attractive alternative for initial assessment and serial monitoring of patients with chronic hepatitis-C.

Limitations of Study

Several limitations should be acknowledged in interpreting these results. The operator-dependent nature of Doppler ultrasound may introduce variability in diagnostic performance across different healthcare settings.

Another limitation of our study is that radiologists were not blinded to the patients' HCV status, which could have introduced observer bias.

Histopathology, while the gold standard, is subject to sampling variability.

Additionally, our study was conducted at a single center, which may limit the generalizability of findings to other populations or healthcare systems.

Future multi-center studies with standardized protocols would strengthen the evidence base for clinical implementation.

Conclusion

Our study confirms that Doppler ultrasound is a highly sensitive and moderately specific tool for detecting cirrhosis in hepatitis C patients. Its ability to detect early hemodynamic changes supports its integration into clinical practice as an adjunct to liver biopsy, particularly in resource-limited settings. These findings contribute to the growing body of literature advocating for the use of non-invasive imaging in managing chronic liver disease.

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Data acquisition, analysis and interpretation	HF, SN, LK
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All the authors agree to take responsibility for every facet of the work, making sure that any concerns about its integrity or veracity are thoroughly examined and addressed.	