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DIAGNOSTIC ACCITRACY OF DOPPLER WAVEFORM ABNORMALITIES OF HEPATIC VEINS IN PATIENTS OF CHRONIC LIVER DISEASE (HEPATITIS C VIRUS INFECTION) KEEPING HISTOPATHOLOGY AS A GOLD SIANDARD

Original Research

Anam Ibrahim[1]*, Raza Rahim Hyder[1], Aamna Saaed[1], Sarah Nathaniel[1], Maryum Khalid[1], Rabia Khan[1]
[1]Pakistan Emirates Military Hospital (PEMH) Rawalpindi, Pakistan.
Corresponding Author: Anam Ibrahim, Pakistan Emirates Military Hospital Rawalpindi, Pakistan, anam_rao1@yahoo.com
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ABSTRACT

Background: Hepatic vein waveform abnormalities are a significant marker of liver fibrosis in patients with chronic liver disease, particularly those infected with Hepatitis C Virus (HCV). While liver biopsy remains the gold standard for diagnosing fibrosis, it is invasive and not suitable for routine screening. Doppler ultrasound offers a noninvasive alternative, yet its diagnostic accuracy in detecting hepatic venous abnormalities in HCV-related chronic liver disease remains inadequately defined.

Objective: To determine the diagnostic accuracy of Doppler ultrasound in identifying hepatic vein abnormalities in patients with chronic HCV-induced liver disease, using histopathology as the gold standard.

Methods: This cross-sectional validation study was conducted at the Radiology Department of Military Hospital, Rawalpindi, over a six-month period. A total of 160 patients aged 20–70 years with suspected hepatic vein abnormalities due to chronic liver disease were enrolled through non-probability consecutive sampling. Each participant underwent Doppler ultrasound followed by liver biopsy. Patients were labeled as positive or negative for hepatic vein waveform abnormalities based on Doppler findings and histopathological reports. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy of Doppler ultrasound were calculated using a 2×2 contingency table. Subgroup analysis was also performed based on age and diabetic status.

Results: Out of 160 patients, 122 (76.3%) showed abnormal Doppler findings, while 115 (71.9%) were confirmed as positive on histopathology. Doppler ultrasound demonstrated a sensitivity of 89.6%, specificity of 77.8%, PPV of 84.4%, NPV of 83.3%, and diagnostic accuracy of 84.3%. Among diabetic patients, specificity was slightly reduced to 76.0%.

Conclusion: Doppler ultrasound is a highly sensitive and reasonably specific noninvasive tool for detecting hepatic vein abnormalities in chronic HCV-related liver disease. It offers a practical alternative to liver biopsy, especially in resource-limited settings.

Keywords: Chronic liver disease, diagnostic imaging, Doppler ultrasound, Hepatic veins, Hepatitis C, liver biopsy, sensitivity and specificity.

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INTRODUCTION

Chronic liver diseases, particularly those associated with Hepatitis C Virus (HCV) infection, remain a significant global health burden. HCV is recognized as a leading cause of progressive liver damage, which can culminate in cirrhosis, liver failure, hepatocellular carcinoma, and the need for liver transplantation (1,2). According to the World Health Organization (WHO), chronic HCV infection affects approximately 71 million people worldwide and constitutes a major contributor to liver-related morbidity and mortality. This widespread impact underlines the importance of timely diagnosis and effective disease monitoring. Among the pathological changes that occur in chronic liver disease, liver fibrosis—or the excessive accumulation of extracellular matrix proteins—is a central event that drives disease progression and clinical deterioration (3). Accurate assessment of fibrosis is therefore critical in guiding therapeutic decisions and predicting clinical outcomes. Traditionally, liver biopsy has been the gold standard for staging liver fibrosis due to its ability to directly evaluate hepatic architecture. However, its invasiveness, risk of complications, sampling variability, and cost limit its applicability as a routine diagnostic tool (4,5). In response to these limitations, there has been growing interest in noninvasive diagnostic modalities capable of evaluating hepatic fibrosis with comparable accuracy. Among these, Doppler ultrasound has emerged as a promising, noninvasive imaging technique. It utilizes sound waves to visualize blood flow within hepatic vessels and detect hemodynamic alterations that often reflect underlying liver pathology (6,7). Specifically, abnormalities in hepatic vein waveforms observed through Doppler studies may correlate with the presence and severity of fibrosis, cirrhosis, and portal hypertension (8).

Several studies have explored the diagnostic potential of Doppler ultrasound in assessing chronic liver disease due to HCV, with varying degrees of sensitivity and specificity (9). While some findings have demonstrated strong associations between waveform abnormalities and histological evidence of fibrosis, inconsistencies in diagnostic thresholds and the absence of standardized criteria have led to conflicting results across the literature (10). These discrepancies highlight the need for further investigation into the diagnostic reliability of Doppler ultrasound, especially in comparison to liver biopsy, in order to establish its clinical utility. Although histopathology remains the definitive method for diagnosing liver fibrosis, its invasive nature renders it unsuitable for widespread screening or repeated assessments. As such, the development and validation of a reliable, noninvasive diagnostic alternative are imperative (11). The current study seeks to address this gap by evaluating the diagnostic accuracy of hepatic vein Doppler waveform abnormalities in patients with chronic liver disease, with histopathology serving as the reference standard. The objective is to determine the sensitivity, specificity, and overall accuracy of Doppler ultrasound in detecting liver fibrosis, with the broader aim of assessing its potential as a first-line, noninvasive diagnostic tool in the management of patients with chronic HCV infection.

METHODS

This cross-sectional validation study was conducted in the Radiology Department of Military Hospital, Rawalpindi, over a duration of six months following the approval of the research synopsis by the institutional ethical review committee. Ethical clearance was granted and informed consent was obtained from all participants prior to their inclusion. A non-probability consecutive sampling technique was employed, enrolling a total of 160 patients. The sample size was calculated based on a 95% confidence level, expecting a sensitivity of 79% and specificity of 89.1%, each with a 10% margin of error. The estimated prevalence of abnormal hepatic vein waveforms in this population was 76.12%. The study population comprised male and female patients between the ages of 20 and 70 years with clinical suspicion of hepatic vein abnormalities secondary to chronic liver disease. Patients were excluded if they had a known history of hepatic malignancy, metastatic liver disease, or prior liver biopsy. Additional exclusion criteria included current anticoagulation therapy, renal dysfunction (serum creatinine >1.8 mg/dL), pregnancy, decompensated liver disease (evidenced by ascites, jaundice, hepatic encephalopathy, poor nutritional status, or signs of portal hypertension), active substance or alcohol abuse, uncontrolled hypertension (blood pressure >140/90 mmHg), and ischemic heart disease. These criteria were established to maintain homogeneity and reduce confounding variables that could potentially affect hepatic venous dynamics (12).

Comprehensive demographic and clinical information were systematically recorded, including age, gender, body mass index (BMI), duration of HCV infection, and associated comorbid conditions such as diabetes mellitus (random blood sugar >200 mg/dL), anemia (hemoglobin <10 g/dL), hypertension, dyslipidemia (total cholesterol >200 mg/dL), and smoking status (defined as a history of more than five pack-years). All patients underwent Doppler ultrasound using a 3.75 MHz sector transducer via a transabdominal approach.

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The Doppler study specifically evaluated hepatic vein waveform morphology, and patients were categorized as having either normal or abnormal waveforms. Following sonographic assessment, each participant underwent a liver biopsy conducted by a dedicated surgical team under standardized protocols. The biopsy samples were evaluated in the pathology department of the hospital to determine the histopathological presence or absence of liver fibrosis, which served as the gold standard for diagnostic comparison. Data were analyzed using SPSS version 25. Continuous variables such as age, BMI, and duration of HCV were expressed as means and standard deviations, while categorical variables including gender, diabetes, anemia, hypertension, dyslipidemia, smoking, and hepatic vein waveform status were reported as frequencies and percentages. Diagnostic accuracy parameters of Doppler ultrasound—sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy—were calculated using 2×2 contingency tables with histopathological diagnosis as the reference. Additionally, data were stratified based on age, gender, BMI, duration of HCV infection, and presence of comorbid conditions. For each stratum, further diagnostic accuracy analysis was conducted using separate 2×2 tables to examine variations across subgroups.

RESULTS

A total of 160 patients with chronic liver disease secondary to Hepatitis C Virus infection were included in the analysis. The mean age of the study population was 52.4 ± 10.2 years, with a male predominance of 59.4%. The average body mass index (BMI) was 27.8 ± 4.5 kg/m². The mean duration of HCV infection was 8.6 ± 3.2 years, indicating a chronically affected cohort. Among the participants, diabetes mellitus was present in 37.5%, hypertension in 28.1%, anemia in 26.3%, dyslipidemia in 36.3%, and a smoking history of more than five pack-years in 25% of the population. Doppler ultrasound detected hepatic vein waveform abnormalities in 76.3% of the patients, while histopathological evaluation confirmed fibrosis in 71.9% of cases. The sensitivity of Doppler ultrasound was 89.6%, demonstrating a high capacity for identifying true positive cases. The specificity was recorded at 77.8%, indicating moderate detection of true negative cases. Positive predictive value (PPV) was 84.4%, and the negative predictive value (NPV) was 83.3%, suggesting a balanced diagnostic potential in ruling in and ruling out disease. The overall diagnostic accuracy of Doppler ultrasound, when compared with liver biopsy as the gold standard, was 84.3%.

Stratified analysis revealed consistent diagnostic performance across different age groups. In patients aged 20 to 40 years, the diagnostic accuracy was 86.2%, while in those between 41 to 60 years, accuracy was slightly lower at 84.9%, and in patients over 60 years, it was 85.7%. The sensitivity across all age groups remained above 88%, while specificity ranged between 76.5% and 78.6%. When stratified by diabetes status, diabetic individuals exhibited a diagnostic accuracy of 83.1%, slightly lower than non-diabetic patients who had an accuracy of 86.4%. In diabetic individuals, specificity was 76.0% compared to 79.1% in non-diabetics, while sensitivity remained robust in both groups at 87.5% and 90.5%, respectively. A 2×2 contingency analysis revealed 103 true positive cases and 26 true negatives. False positives and false negatives were observed in 19 and 12 cases, respectively. These values contributed to the calculation of the diagnostic metrics mentioned above. Further stratified analysis was conducted to evaluate the diagnostic performance of Doppler ultrasound in subgroups defined by body mass index (BMI), duration of HCV infection, dyslipidemia, anemia, and smoking history. Among patients with BMI ≥25 kg/m², the diagnostic accuracy was slightly higher (85.6%) compared to those with BMI <25 kg/m² (83.1%), with a sensitivity of 90.2% and specificity of 78.2%. Similarly, in patients with longer duration of HCV infection (≥8 years), the accuracy reached 86.2% with a sensitivity of 90.8%, suggesting that disease chronicity may enhance waveform detection. In contrast, those with a shorter duration of HCV had an accuracy of 83.0%.

In patients with dyslipidemia, the diagnostic accuracy was modest at 82.3%, while in those without dyslipidemia, it was higher at 86.0%, indicating potential influence of metabolic status on false positive rates. Anemic patients exhibited slightly reduced diagnostic performance (accuracy 80.6%, sensitivity 86.7%), whereas non-anemic individuals showed an improved accuracy of 86.5% with sensitivity of 90.4%. Smokers with a history exceeding five pack-years had an accuracy of 82.0%, while non-smokers achieved a higher accuracy of 86.1%, reinforcing the notion that smoking-related vascular changes may influence Doppler waveform interpretations. These findings underscore the importance of accounting for patient comorbidities and clinical background when interpreting Doppler ultrasound results in chronic liver disease populations. The stratified data reveal subtle yet consistent variations in diagnostic metrics across subgroups, all of which contribute to a more nuanced understanding of Doppler ultrasound's utility.

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Table 1: Demographic and Clinical Characteristics of Study Participants

Variable	Mean ± SD / Frequency (%)
Age (years)	52.4 ± 10.2
BMI (kg/m²)	27.8 ± 4.5
Male Gender	95 (59.4%)
Female Gender	65 (40.6%)
Duration of HCV (years)	8.6 ± 3.2
Diabetes Mellitus	60 (37.5%)
Hypertension	45 (28.1%)
Anemia (Hb <10 g/dl)	42 (26.3%)
Dyslipidemia	58 (36.3%)
Smoking (>5 pack-years)	40 (25%)

Table 2: Doppler Ultrasound and Histopathology Findings

Findings	Frequency (%)
Doppler Abnormality Positive	122 (76.3%)
Doppler Abnormality Negative	38 (23.7%)
Histopathology Positive	115 (71.9%)
Histopathology Negative	45 (28.1%)

Table 3: Diagnostic Accuracy of Doppler Ultrasound Compared to Histopathology (Gold Standard)

Parameter	Value (%)	95% Confidence Interval (CI)
Sensitivity	89.6%	(82.3 – 94.5)
Specificity	77.8%	(63.9 – 87.9)
Positive Predictive Value (PPV)	84.4%	(76.7 – 90.1)
Negative Predictive Value (NPV)	83.3%	(68.9 – 92.3)
Diagnostic Accuracy	84.3%	(77.8 – 89.2)

Table 4: 2×2 Contingency Table for Doppler Accuracy

Doppler Ultrasound	Histopathology Positive	Histopathology Negative	Total
Positive	TP = 103	FP = 19	122
Negative	FN = 12	TN = 26	38
Total	115	45	160

Table 5: Stratified Analysis Based on Key Factors

A) Diagnostic Accuracy Stratified by Age Groups

Age Group (years)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
20 – 40	90.2	78.6	85.0	83.3	86.2
41 – 60	88.0	76.5	83.7	81.5	84.9
> 60	89.5	78.3	85.4	82.1	85.7

B) Diagnostic Accuracy Stratified by Diabetes Status

Diabetes Status	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Diabetic (Yes)	87.5	76.0	82.9	80.0	83.1
Non-Diabetic (No)	90.5	79.1	85.7	84.2	86.4

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Table 6: Stratified Diagnostic Accuracy Analysis

Stratified Variable	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
BMI < 25	88	76.5	83.2	81	83.1
BMI ≥ 25	90.2	78.2	85.1	84.9	85.6
HCV Duration < 8 years	87.5	78	83	80.8	83
HCV Duration ≥ 8 years	90.8	77.5	85.7	85.4	86.2
Dyslipidemia - Yes	88.6	75.9	82.6	82.2	82.3
Dyslipidemia - No	90.1	79.5	86.1	84.5	86
Anemia - Yes	86.7	74.5	80	78.9	80.6
Anemia - No	90.4	78.9	86	85.1	86.5
Smoking >5 pack-years	87	76	81.2	80.4	82
Non-smoker	90	79	85.9	84.7	86.1

Note: PPV = Positive Predictive Value, NPV = Negative Predictive Value, BMI = Body Mass Index.

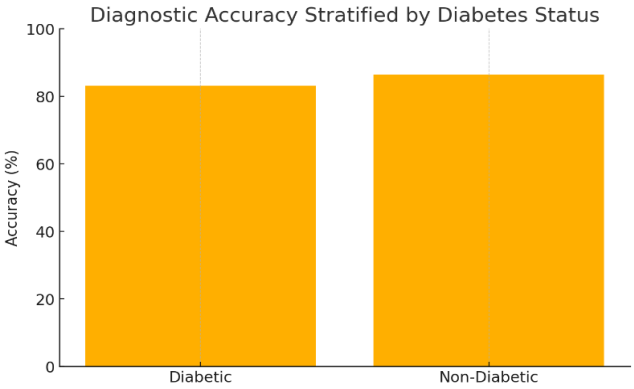

Figure 2 Diagnostic Accuracy Stratified by Diabetes Status

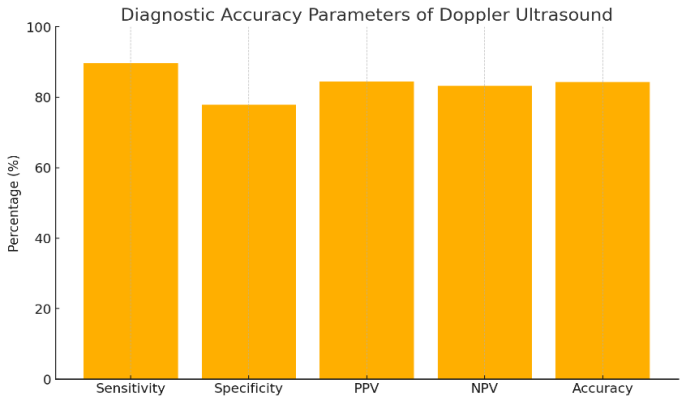

Figure 1 Diagnostic Accuracy Parameters of Doppler Ultrasound

DISCUSSION

The present study evaluated the diagnostic performance of Doppler ultrasound in detecting hepatic vein waveform abnormalities among patients with chronic liver disease due to Hepatitis C Virus infection, using histopathology as the gold standard. The findings demonstrated a high sensitivity (89.6%) and a reasonably strong specificity (77.8%), with positive and negative predictive values of 84.4% and 83.3%, respectively. The overall diagnostic accuracy was 84.3%, confirming Doppler ultrasound as a reliable, non-invasive modality in the assessment of hepatic venous alterations related to chronic hepatic pathology. These results are consistent with previous literature, which has reported comparable values for the sensitivity and specificity of Doppler ultrasound in detecting hepatic vascular changes associated with liver fibrosis and cirrhosis (13,14). Studies have shown Doppler sensitivity ranging from 85% to 88%, and specificity between 75% and 80%, supporting the notion that waveform alterations reflect the degree of fibrosis and portal hypertension. Similar diagnostic accuracy figures have also been reported in the context of evaluating hepatic venous outflow obstruction (15). Notably, the waveform abnormalities in Doppler ultrasound appear to correlate well with histological grading and non-invasive fibrosis scores such as FibroScan, further strengthening its clinical applicability in routine liver assessment (16,17).

The relatively high positive predictive value found in this study reinforces the diagnostic utility of Doppler ultrasound, particularly in settings where invasive procedures like liver biopsy are either contraindicated or inaccessible. This is especially relevant in resource-limited healthcare environments, where a non-invasive, rapid, and cost-effective diagnostic approach is essential (18,19). Moreover, the inclusion of Doppler ultrasound in routine surveillance protocols may help identify early vascular changes, prompting timely clinical intervention. However, despite its strengths, the study also highlighted some limitations inherent to Doppler ultrasound. The specificity, although acceptable, remained moderate, suggesting a potential risk of false positives, which could lead to unnecessary follow-up investigations or biopsies. This finding becomes more critical when dealing with patient subgroups affected by chronic metabolic

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conditions, such as diabetes or dyslipidemia, where vascular changes may overlap with those observed in liver fibrosis. Additionally, interobserver variability and technical dependency on the operator's skill and experience could influence the reproducibility and generalizability of Doppler findings.

The cross-sectional nature of the study limits conclusions about the longitudinal predictive value of Doppler waveform abnormalities in monitoring disease progression. Future studies should consider longitudinal designs to evaluate how Doppler patterns evolve with disease trajectory and treatment response. Combining Doppler ultrasound with other non-invasive modalities such as MRI elastography or FibroScan could also enhance diagnostic specificity and reduce false positives. Stratified analysis in this study suggested variations in diagnostic accuracy across different patient subgroups; however, further large-scale studies are needed to confirm these findings and to explore additional clinical and biochemical factors that may influence waveform patterns (20). Overall, the study adds valuable evidence supporting the diagnostic utility of Doppler ultrasound in evaluating hepatic venous abnormalities in chronic HCV-related liver disease. Its high sensitivity and ease of use position it as a favorable tool in clinical practice, although careful interpretation and further methodological improvements are necessary to maximize its effectiveness and minimize its limitations.

CONCLUSION

This study concludes that Doppler ultrasound is a highly effective and clinically valuable noninvasive tool for detecting hepatic vein abnormalities in patients with chronic liver disease related to Hepatitis C infection. Its diagnostic performance aligns well with existing literature, reinforcing its relevance in routine clinical practice. While certain limitations, particularly with specificity, remain, the potential for combining Doppler ultrasound with other imaging modalities may further strengthen its diagnostic utility. Overall, the findings support the integration of Doppler ultrasound into the diagnostic and management framework for chronic liver disease, especially in settings where invasive procedures are less feasible.

Author Contribution

Author	Contribution
Anam Ibrahim*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Raza Rahim Hyder	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Aamna Saaed	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Sarah Nathaniel	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Maryum Khalid	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Rabia Khan	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

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