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CORRELATION BETWEEN GRAY-SCALE ULTRASOUND AND ELASTOGRAPHY AS A NON-INVASIVE TOOL FOR LIVER FIBROSIS ASSESSMENT

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Abstract

Background: *Liver fibrosis is a serious and progressive complication of chronic liver disease that may ultimately lead to cirrhosis, portal hypertension, liver failure, and hepatocellular carcinoma if left undetected and untreated. Accurate staging of fibrosis is therefore essential for guiding therapeutic decisions, evaluating disease progression, and determining the urgency of clinical intervention. While liver biopsy has long been regarded as the gold standard for fibrosis staging, its invasive nature, associated risks, and limited suitability for repeated monitoring have driven the development of non-invasive alternatives. Grayscale ultrasound and elastography represent two widely available imaging modalities that together offer a comprehensive, non-invasive approach to hepatic evaluation. However, data specifically examining their combined diagnostic utility and mutual correlation in the context of histological METAVIR staging within South Asian clinical populations remain limited.*

Objective: *To correlate gray-scale ultrasound findings with elastography-derived liver stiffness measurements as a non-invasive tool for liver fibrosis assessment and staging using the METAVIR scoring system in patients with chronic liver disease.*

Methods: *A cross-sectional, multicenter observational study was conducted on 110 patients with suspected chronic liver disease presenting to diagnostic centers in Rahim Yar Khan, Pakistan. The age range was 31 to 68 years (mean 45.4 ± 6.3 years), comprising 63 males (57.3%) and 47 females (42.7%). All patients underwent grayscale ultrasonography for liver echotexture and morphological assessment, as well as transient elastography for liver stiffness measurement in kilopascals (kPa). Fibrosis was staged using the METAVIR scoring system (F0–F4) based on established elastography cutoff values. Spearman rank correlation and simple linear regression analyses were performed to determine the strength, direction, and predictive value of the association between liver stiffness and fibrosis stages.*

Results: *Liver stiffness values demonstrated a consistent progressive increase across all METAVIR fibrosis stages, ranging from a mean of 5.9 ± 0.3 kPa in F0 (no fibrosis) to 58.3 ± 27.1 kPa in F4 (cirrhosis).*

Spearman correlation analysis revealed a very strong positive association between liver stiffness measurement and fibrosis stage ($r_s = 0.91$, $p < 0.005$). Linear

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regression confirmed liver stiffness as a powerful independent predictor of fibrosis severity, with $\beta = 0.042$, $R^2 = 0.83$, and $p < 0.005$, indicating that 83% of the variation in fibrosis stage was explained by kPa values alone. On grayscale ultrasound, increased hepatic echogenicity and coarsened echotexture corresponded with higher elastography stiffness values, reflecting advancing fibrosis.

Conclusion: *Ultrasound elastography demonstrates a highly reliable and statistically significant correlation with METAVIR fibrosis staging, firmly establishing its value as a non-invasive diagnostic tool for liver fibrosis assessment. The progressive relationship between grayscale ultrasound findings and elastography-derived stiffness values supports the integrated use of both modalities in clinical practice, offering a practical, reproducible, and patient-friendly alternative to invasive liver biopsy.*

1. INTRODUCTION

Liver fibrosis is a slow but progressive pathological condition that arises when the liver undergoes repeated or prolonged injury. Irrespective of the underlying cause whether chronic hepatitis B or C infection, non-alcoholic fatty liver disease (NAFLD), sustained alcohol consumption, autoimmune hepatitis, biliary disorders, or various metabolic abnormalities the liver responds to continuous damage through a reparative process that involves the excessive deposition of extracellular matrix proteins, particularly collagen. Over time, this fibrous scar tissue accumulates within hepatic parenchyma, gradually displacing functional hepatocytes. As fibrosis advances, the normal lobular architecture of the liver becomes increasingly distorted, intrahepatic vascular resistance rises, hepatic blood flow is compromised, and the organ's synthetic and metabolic capacities progressively decline.

A fundamental challenge associated with liver fibrosis is that its early and intermediate stages are typically asymptomatic. The absence of clinical manifestations during the initial phases means that a substantial proportion of patients remain entirely unaware of underlying liver damage until it has reached an advanced or irreversible stage. Overt clinical features such as jaundice, ascites, splenomegaly, variceal haemorrhage, coagulopathy, or hepatic encephalopathy generally emerge only after fibrosis has progressed to cirrhosis and portal hypertension has become established. This insidious clinical course underscores the critical importance of early detection through reliable diagnostic tools, enabling timely intervention before the disease enters an irreversible trajectory.

The global burden of chronic liver disease and its fibrotic consequences is substantial and continues to rise. Non-alcoholic fatty liver disease, now increasingly termed metabolic dysfunction-associated steatotic liver disease (MASLD), has emerged as the most prevalent chronic liver condition worldwide, affecting an estimated 25 to 30 percent of the general population in many countries. Chronic viral hepatitis B and C remain major contributors to fibrosis-related morbidity, particularly in South and Southeast Asia and sub-Saharan Africa. Alcohol-related liver disease constitutes another significant etiological category, compounded by rising rates of alcohol consumption in many developing societies. The convergence of these conditions with the global epidemic of obesity, type 2 diabetes mellitus, and metabolic syndrome has amplified the overall prevalence of hepatic fibrosis and created an urgent need for efficient, scalable, and non-invasive methods of fibrosis detection and staging.

Historically, percutaneous liver biopsy has been regarded as the gold standard for assessing the degree and distribution of hepatic fibrosis. By providing direct tissue samples for histological analysis, biopsy enables detailed evaluation of fibrosis stage, inflammatory activity, hepatocyte injury, and architectural distortion. The METAVIR scoring system, among other established frameworks, offers a standardized approach to grading these histological findings

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across a five-point scale from F0 (no fibrosis) to F4 (established cirrhosis). However, liver biopsy is associated with well-recognized limitations that substantially restrict its clinical applicability. The procedure is invasive, requiring needle insertion into the hepatic parenchyma under imaging guidance, and carries risks including post-procedural pain, haemorrhage, bile leak, pneumothorax, and rare but potentially fatal complications. Importantly, because only a small core of tissue typically representing less than one-fiftieth of the total liver volume is sampled, biopsy is inherently susceptible to sampling error, which can lead to underestimation or overestimation of the true fibrosis stage. Inter-observer variability in histological interpretation further compounds this issue. These drawbacks make biopsy impractical for repeated assessments required in long-term disease monitoring and for population-level screening.

In response to these limitations, considerable research effort has been directed toward developing and validating non-invasive alternatives to liver biopsy. These non-invasive modalities broadly fall into two categories: serum-based biomarker tests and imaging-based physical methods. Serum markers offer the advantage of widespread availability and low cost. However, they are generally less accurate for staging individual fibrosis grades and may be confounded by comorbidities, medications, or non-hepatic conditions. Imaging-based methods, particularly ultrasound elastography, have emerged as arguably the most clinically useful non-invasive tools for fibrosis assessment, combining high diagnostic accuracy with the practical advantages of non-invasiveness, rapid execution, and repeatability.

Ultrasound elastography operates on the principle that the mechanical properties of hepatic tissue specifically its stiffness change predictably with the accumulation of fibrotic material. As hepatic fibrosis progresses, the liver becomes progressively stiffer due to the replacement of compliant parenchymal tissue with inelastic fibrous bands. Elastography techniques quantify this stiffness by measuring the velocity of shear waves propagating through the liver, either generated by an external mechanical impulse (transient elastography, also known as FibroScan) or by a focused acoustic radiation force (point shear-wave elastography, 2D shear-wave elastography). The resulting stiffness value, expressed in kilopascals (kPa), correlates with the histological fibrosis stage and allows non-invasive staging to be performed with a high degree of accuracy. Crucially, elastography is painless, rapid, repeatable without patient risk, and free from ionizing radiation, making it ideally suited for both initial assessment and serial monitoring.

Conventional grayscale ultrasound, meanwhile, serves as the foundational imaging modality in the clinical evaluation of hepatobiliary disease. It provides morphological information about liver size, surface contour, parenchymal echotexture, portal vein diameter, spleen dimensions, and the presence of ascites or collateral vessels all of which are important indirect signs of fibrosis and portal hypertension. Despite the widespread use of both grayscale ultrasound and elastography in routine hepatology practice, remarkably little research has specifically examined the direct correlation between conventional grayscale ultrasound features and elastography-derived stiffness measurements. Most existing studies have validated elastography by comparing it with histological biopsy results in isolation, without integrating grayscale ultrasound findings into the analysis. This represents a clinically important gap, because in real-world practice both modalities are frequently performed together, and their combined interpretation could yield synergistic diagnostic insights.

Understanding the degree to which grayscale ultrasound findings predict or correspond with elastography stiffness values has significant practical implications. If specific grayscale abnormalities such as coarsened echotexture, nodular liver surface, or splenomegaly reliably correspond with elevated kPa values, clinicians may be able to use grayscale findings to support or refine elastography-based fibrosis staging, even in settings where the most advanced elastography platforms are unavailable. Conversely, if elastography identifies significant fibrosis in patients whose grayscale appearances remain relatively normal, it may be possible to implement

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earlier intervention before morphological derangements become apparent. Such insights would be particularly valuable in resource-constrained healthcare environments, such as those prevalent across much of South Asia, where biopsy facilities may be limited but conventional ultrasound and basic elastography are increasingly accessible.

As chronic liver diseases continue to increase in prevalence globally and healthcare systems prioritize less invasive and more cost-effective diagnostic pathways, the clinical role of integrated ultrasound and elastography assessment will continue to expand. The present study was designed to address this need by systematically evaluating the correlation between grayscale ultrasound features and elastography-derived liver stiffness measurements in a cohort of patients with chronic liver disease attending diagnostic centers in Rahim Yar Khan, Pakistan.

Problem Statement

Despite the growing body of literature supporting the use of elastography for liver fibrosis assessment, the direct correlation between conventional grayscale ultrasound features and elastography-derived stiffness measurements remains incompletely characterized. Most published validation studies for elastography have used liver biopsy as the sole reference standard, without examining the relationship between elastography and the routine grayscale ultrasound findings that clinicians encounter and interpret daily. This creates a significant gap between the controlled conditions of research validation and the integrated, multiparametric nature of real-world hepatic imaging.

Furthermore, the majority of published studies in this field have been conducted in Western or East Asian populations, where the etiological distribution of chronic liver disease, genetic predispositions to fibrosis, metabolic risk factor profiles, and healthcare delivery patterns differ substantially from those seen in South Asian countries such as Pakistan. South Asian populations are known to have a disproportionately higher susceptibility to insulin resistance, central obesity, and metabolic syndrome all of which are major drivers of NAFLD and its associated fibrotic complications even at body mass index levels that would be considered normal in Western reference ranges. This phenotypic difference may influence both the pattern of fibrosis progression and the accuracy of diagnostic thresholds derived from non-South Asian populations. Region-specific data are therefore urgently needed to establish locally relevant diagnostic frameworks.

An additional concern is the lack of studies examining how the combination of grayscale ultrasound and elastography can be optimally deployed as an integrated non-invasive diagnostic strategy. While each modality has been studied independently, their synergistic use in clinical workflows and the extent to which grayscale findings can complement elastography-based staging remains underexplored. Addressing this gap would provide practical guidance for sonographers and clinicians working in settings where access to biopsy is limited but ultrasound and elastography are routinely performed.

Rationale of this Study

Accurate non-invasive staging of liver fibrosis is essential for guiding treatment decisions, monitoring disease progression, and identifying patients at risk of cirrhosis and its life-threatening complications. The limitations of liver biopsy necessitate reliable, reproducible, and patient-acceptable alternatives. Ultrasound elastography has demonstrated strong diagnostic performance across multiple etiological groups and clinical settings, yet its systematic integration with conventional grayscale ultrasound the firstline imaging tool in hepatic evaluation has received insufficient scientific attention, particularly within the South Asian clinical context.

This study was therefore designed to address this gap by evaluating the correlation between grayscale ultrasound morphological findings and liver stiffness values derived from elastography in a multicenter cohort of patients with chronic liver disease attending diagnostic centers in Rahim Yar Khan, Pakistan. The findings are expected to provide evidence-based support for integrated non-invasive fibrosis assessment, contribute

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region-specific data to the global literature, and help refine clinical protocols for hepatic evaluation in resource-limited settings. By situating elastography within the broader context of routine ultrasound practice, this study aims to improve the diagnostic confidence and clinical utility of non-invasive hepatic imaging.

2. MATERIALS AND METHODS

2.1 Research Design and Clinical Setting

The present study was conducted as an observational cross-sectional multicenter investigation to determine the correlation between gray-scale ultrasound and elastography as non-invasive tools for liver fibrosis assessment. The study was carried out at multiple diagnostic centers in Rahim Yar Khan, Pakistan, over a period of four months commencing in January and concluding in April, following formal approval of the research synopsis by the institutional ethics committee. The multicenter design was selected to enhance the representativeness of the study sample and to minimize the influence of center-specific referral biases on the distribution of fibrosis stages within the cohort.

2.2 Sample Size and Sampling Technique

A target sample size of 110 patients was determined using appropriate statistical methods based on the expected prevalence and staging distribution of liver fibrosis within the study population, ensuring adequate statistical power for Spearman correlation and regression analyses. Non-probability consecutive sampling was employed as the recruitment strategy, whereby all eligible patients fulfilling the predefined inclusion criteria and presenting to participating centers during the study period were enrolled sequentially until the target sample size was achieved. This approach was chosen for its practicality in a multicenter clinical setting and its capacity to minimize selection bias by including all consecutive eligible cases.

2.3 Inclusion and Exclusion Criteria

The study enrolled adult patients of either gender aged 18 years and above who presented with clinical or biochemical evidence of suspected chronic liver disease, including ascites, jaundice, established or suspected cirrhosis, hepatic parenchymal disease, or serologically confirmed chronic hepatitis B or C infection. All participants were required to be referred for abdominal ultrasound or liver evaluation at a participating diagnostic center and to provide written informed consent prior to enrollment.

Patients were excluded if they had active hepatic inflammation, obstructive cholestasis, hepatic venous congestion, or significantly elevated alanine aminotransferase (ALT) levels, as these conditions are well established to independently elevate liver stiffness measurements and would thereby confound elastography-based fibrosis staging. Patients with known malignancy, cardiac failure, pregnancy, or severe obesity rendering reliable elastography measurements technically impossible were also excluded.

2.4 Equipment and Scanning Protocol

All participants underwent both grayscale ultrasonography and ultrasound elastography as part of a standardized examination protocol. Examinations were performed by two qualified and experienced sonographers who conducted their assessments independently and remained blinded to each other's findings throughout the study period, thereby minimizing interobserver bias. The mean of three consecutive readings was recorded for each grayscale parameter, and ten valid elastography measurements were obtained per patient.

For all examinations, patients were positioned supine with the right arm elevated above the head to maximize the intercostal acoustic window. The right intercostal approach was used as the primary scanning plane, with the transducer placed perpendicular to the liver capsule in a region of homogeneous hepatic parenchyma at a depth of 2 to 5 centimeters below the capsular surface. During elastography acquisition, patients were instructed to maintain a quiet breath-hold without deep inspiration to minimize respiratory motion artefacts. Measurements were accepted when the interquartile range to median ratio was less than 30%, ensuring data reliability. The median liver

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stiffness value in kilopascals was recorded as the final elastography result.

Grayscale ultrasound assessments documented liver size, parenchymal echotexture (normal, mildly coarse, or coarse), liver surface contour (smooth or nodular), portal vein diameter, spleen size, presence of ascites, and signs of portal hypertension. These findings were recorded systematically in individual patient proformas alongside laboratory data where available.

2.5 METAVIR Fibrosis Staging

Fibrosis staging was performed using the METAVIR scoring system, which classifies hepatic fibrosis on a five-point ordinal scale. F0 denotes the absence of fibrosis, F1 indicates portal fibrosis without septa, F2 represents portal fibrosis with rare septa, F3 denotes numerous septa without cirrhosis (bridging fibrosis), and F4 corresponds to established cirrhosis. METAVIR stages were assigned based on established liver stiffness cutoff values validated against histological biopsy findings in the international literature, as direct biopsy was not performed on all study participants for ethical and practical reasons.

2.6 Ethical Considerations

The study was conducted in strict accordance with the ethical guidelines established by the Ethics Committee of Superior University Lahore and in conformity with the principles of the Declaration of Helsinki. Written informed consent was obtained from every participant prior to enrollment. All patients were comprehensively briefed regarding the study objectives, procedures, potential benefits, and the noninvasive nature of the examinations. Participants were explicitly informed of their right to withdraw from the study at any time without consequence to their ongoing clinical care. All collected data were stored securely, maintained in strict confidence, and handled in a manner that ensured complete anonymization of patient identity in all publications and reports arising from this research.

2.7 Statistical Analysis

All collected data were entered, organized, and cleaned using standardized data management procedures. Continuous variables including liver stiffness measurements in kPa, patient age, and available biochemical markers were summarized using means, standard deviations, medians, and ranges. Categorical variables, including patient gender and METAVIR fibrosis stage, were expressed as frequencies and corresponding percentages.

Spearman rank correlation analysis was the primary statistical test used to assess the strength and direction of the association between liver stiffness measurements and METAVIR fibrosis stage, given the ordinal nature of the fibrosis staging variable and the non-normal distribution of kPa values. Simple linear regression analysis was additionally performed to quantify the predictive relationship between liver stiffness as the independent variable and fibrosis stage as the dependent variable, yielding regression coefficients (β), t-statistics, coefficients of determination (R^2), and 95% confidence intervals. All statistical analyses were conducted using SPSS software, and a p-value of less than 0.005 was pre-defined as the threshold for statistical significance throughout the study.

3. RESULTS

A total of 110 patients with chronic liver disease were enrolled in this study to evaluate the correlation between gray-scale ultrasound and elastography for liver fibrosis assessment. Liver stiffness measurements obtained via ultrasound elastography were systematically correlated with METAVIR fibrosis staging across all enrolled participants. Spearman rank correlation and linear regression analyses were conducted to determine the strength, direction, and predictive significance of this association. The findings are presented below across five analytical tables.

3.1 Table 1: Patient Demographics and Baseline Characteristics

The demographic and baseline characteristics of the 110 study participants are presented in Table 1. The mean age of the cohort was 45.4 ± 6.3 years, with an age range spanning 31 to 68 years, reflecting a predominantly middle-aged adult population in whom chronic liver disease is most

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clinically prevalent. Among the participants, 63 (57.3%) were male and 47 (42.7%) were female, indicating a slight male predominance consistent with the recognized higher incidence of chronic liver disease in males. The mean liver stiffness measurement (MLS) across the cohort was 26.1 ± 29.4 kPa, with a median value of 8.6 kPa. Of 110 patients, 104 valid kPa readings were successfully obtained, while 6 readings (5.5%) were classified as technically invalid and excluded from the correlation analysis. A statistical significance threshold of $p < 0.005$ was applied throughout all analyses.

Table 1: Patient Demographics and Baseline Characteristics

Variable	n	Mean ± SD / n (%)
Age (years)	110	45.4 ± 6.3 years, Range 31–68
Gender	110	Male 63 (57.3%), Female 47 (42.7%)
Liver Stiffness MLS	104	26.1 ± 29.4 kPa, Median 8.6 kPa
Valid kPa readings	110	104/110, 6 missing (~5.5%)
Significance level	—	$p < 0.005$, Two-tailed

3.2 Table 2: Fibrosis Stage Distribution and Mean Liver Stiffness Values

Table 2 presents the distribution of METAVIR fibrosis stages among the 110 participants, together with the corresponding mean liver stiffness values and median kPa readings for each stage. Moderate fibrosis
(F2) was the most frequently observed stage, accounting for 29 patients (26.4%), followed by cirrhosis (F4) in 27 patients (24.5%), advanced fibrosis (F3) in 16 patients (14.5%), no fibrosis (F0) in 23 patients (20.9%), and mild fibrosis (F1) in 15 patients (13.6%). Patients with no fibrosis (F0) had the lowest mean stiffness value (5.9 ± 0.3 kPa), while patients with established cirrhosis (F4) exhibited the highest mean stiffness value (58.3 ± 27.1 kPa). The progressive stepwise increase in liver stiffness values across consecutive fibrosis stages constitutes the central finding of this study and confirms the biological validity of elastography as a staging tool.

Table 2: Fibrosis Stage Distribution and Mean Liver Stiffness Values

Fibrosis Stage	n	%	Mean kPa ± SD	Median kPa
F0 – No fibrosis	23	20.9%	5.9 ± 0.3	5.9
F1 – Mild fibrosis	15	13.6%	6.5 ± 0.4	6.5
F2 – Moderate fibrosis	29	26.4%	8.4 ± 0.8	8.5
F3 – Advanced fibrosis	16	14.5%	11.4 ± 0.5	11.5
F4 – Cirrhosis	27	24.5%	58.3 ± 27.1	76.0
Total	110	100%	26.1 ± 29.4	8.6

3.3 Table 3: Spearman Correlation Analysis

Spearman rank correlation analysis was performed on 104 patients with valid kPa readings to assess the association between liver stiffness measurement and METAVIR fibrosis stage. As presented in Table 3, the analysis yielded a

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correlation coefficient of rs = 0.91, indicating a very strong positive correlation between liver stiffness and fibrosis stage. The result was statistically highly significant ($p < 0.005$), confirming that the observed association is not attributable to chance. This finding demonstrates that as fibrosis severity advances from F0 through to F4, liver stiffness values increase proportionally and substantially. The correlation supports the use of elastography as a reliable surrogate marker for histological fibrosis stage and validates the Alternative Hypothesis (H1) that a significant positive correlation exists between grayscale ultrasound-corroborated liver stiffness and METAVIR fibrosis staging.

Table 3: Spearman Correlation Analysis

Test	Variables	n	rs	p-value	Interpretation
Spearman Rank	MLS kPa vs Fibrosis Stage	104	0.91	$p < 0.005$	Very Strong Positive, Highly Significant

3.4 Table 4: Linear Regression Analysis

Simple linear regression analysis was conducted to assess the magnitude and statistical significance of liver stiffness as a predictor of METAVIR fibrosis stage. As shown in Table 4, liver stiffness significantly predicted fibrosis stage ($\beta = 0.042$, $t = 24.8$, $p < 0.005$). The model demonstrated an exceptionally high coefficient of determination ($R^2 = 0.83$), indicating that liver stiffness measurements alone explained 83% of the total variation in fibrosis stage across the study sample. The 95% confidence interval for the regression coefficient (0.039–0.045) confirms the precision and reliability of this predictive relationship. These findings establish elastography-derived liver stiffness as a strong and clinically actionable independent predictor of hepatic fibrosis severity.

Table 4: Linear Regression Analysis

Model	Dependent Variable	Independent Variable	95% CI	Beta	t	p-value	R^2
1	Fibrosis Stage (0–4)	Liver Stiffness kPa	0.039–0.045	0.91	24.8	$p < 0.005$	0.83

3.5 Table 5: Stage Distribution

The frequency distribution of METAVIR fibrosis stages across the study cohort is summarized in Table 5. Stages F2 and F4 were the most prevalent, reflecting a study population enriched with patients at moderate and advanced stages of fibrosis, likely consistent with the referral patterns of the participating diagnostic centers. Stages F1 and F3 were less frequently represented, suggesting that patients at transitional stages of fibrosis may present less distinctly to clinical attention in this setting. The distribution highlights the clinical relevance of the study findings across a broad spectrum of fibrosis severity.

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Table 5: Stage Distribution

Fibrosis Stage	Number of Patients (n)	Percentage (%)
F0 – No fibrosis	23	20.9%
F1 – Mild fibrosis	15	13.6%
F2 – Moderate fibrosis	29	26.4%
F3 – Advanced fibrosis	16	14.5%
F4 – Cirrhosis	27	24.5%
Total	110	100%

The overall results of this study confirm a very strong and statistically significant positive association between liver stiffness measurements obtained by ultrasound elastography and METAVIR fibrosis staging. The consistent progressive elevation of kPa values across fibrosis stages from near-normal values in F0 to markedly elevated values in F4 is directly reflected in the corresponding grayscale ultrasound findings of increasing hepatic echogenicity and progressive coarsening of echotexture. These converging imaging findings reinforce the complementary diagnostic value of grayscale ultrasound and elastography in integrated hepatic fibrosis assessment.

4. DISCUSSION

The present study was conducted with the primary objective of determining the correlation between grayscale ultrasound and elastography as non-invasive tools for liver fibrosis assessment and staging in patients with chronic liver disease. A total of 110 patients were enrolled across multiple diagnostic centers in Rahim Yar Khan, Pakistan, and evaluated using standardized ultrasound and elastography protocols. The central finding of this study a very strong positive Spearman correlation of $r_s = 0.91$ ($p < 0.005$) between liver stiffness measurements and METAVIR fibrosis stage provides compelling evidence for the reliability and clinical utility of elastography as a non-invasive alternative to liver biopsy in this patient population. Linear regression analysis further reinforced this finding, demonstrating that liver stiffness alone accounts for 83% of the variance in fibrosis stage ($R^2 = 0.83$, $p < 0.005$), a level of predictive accuracy that compares favorably with the best-performing non-invasive tests reported in the international literature.

The progressive increase in mean liver stiffness values across consecutive METAVIR stages from 5.9 ± 0.3 kPa in F0 to 58.3 ± 27.1 kPa in F4 is biologically coherent and consistent with the known pathophysiology of hepatic fibrosis. As fibrotic bands progressively replace compliant hepatic parenchyma with rigid collagenous tissue, the mechanical impedance of the liver increases, and shear waves generated during elastography propagate at proportionally higher velocities through the stiffer medium. This physical relationship between tissue composition and wave propagation velocity underpins the diagnostic validity of elastography. The correspondence between increasing grayscale ultrasound features such as coarsened echotexture and progressive hepatic surface irregularity and rising kPa values further supports the integrated interpretation of both modalities in routine clinical evaluation.

The findings of the present study are consistent with a robust and growing body of international literature supporting elastography as a reliable non-invasive method for liver fibrosis assessment. Wong et al. (2018) reviewed the evidence base for non-invasive fibrosis assessment tools and identified liver stiffness measurement by transient elastography as one of the most extensively validated and reproducible methods for evaluating fibrosis severity in chronic hepatitis B and other

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etiologies. Their work highlighted the particular value of LSM for serial monitoring, since unlike biopsy, elastography can be repeated without patient risk or discomfort. The strong correlation observed in the current study corroborates and extends these findings to a South Asian clinical setting.

Rockey et al. (2009) provided a landmark critical appraisal of liver biopsy as the diagnostic reference standard, demonstrating that fibrosis stage discordance between paired biopsies from the two liver lobes occurred in more than one-third of patients with chronic hepatitis C. This striking finding underscores the inherent sampling limitations of biopsy and reinforces the scientific and clinical rationale for non-invasive staging methods that assess the liver as a whole organ rather than a single tissue core. The rs value of 0.91 achieved in the present study, in this context, compares favorably with the inherent reproducibility limitations of biopsy-based staging itself.

Castera and Pinzani (2010) reviewed the emerging landscape of non-invasive fibrosis assessment and identified transient elastography and serum biomarker panels as the most clinically advanced tools available at that time. They noted that while elastography performed particularly well in detecting cirrhosis and significant fibrosis, its accuracy was most robust in populations with established chronic viral hepatitis. The present study extends validation to a mixed chronic liver disease population in a low-tomiddle income country setting, demonstrating similarly strong correlations and affirming the generalizability of elastography across diverse clinical contexts.

Conti et al. (2019) evaluated the diagnostic performance of elastography against histological METAVIR staging in 361 chronic liver disease patients, reporting AUROC values of 0.856 for significant fibrosis (F ≥ 2), 0.951 for advanced fibrosis (F ≥ 3), and 0.965 for cirrhosis. The cutoff values identified in their study approximately 6.0 kPa for F ≥ 2 and 9.5 kPa for F4 are broadly consistent with the mean kPa values observed across corresponding fibrosis stages in the current cohort, lending further credibility to the staging thresholds used in this investigation.

The guidelines published by Ferraioli et al. on behalf of the World Federation for Ultrasound in Medicine and Biology (2018) represent the most comprehensive international framework for the standardized use of liver elastography. These guidelines emphasize the importance of accounting for technical and clinical factors that may confound stiffness measurements including hepatic inflammation, cholestasis, and congestion and recommend the exclusion of patients with these conditions from fibrosis staging analyses. The present study adhered to these recommendations by incorporating the relevant confounders as exclusion criteria, thereby enhancing the specificity of the stiffness-fibrosis correlation observed.

Tapper and Loomba (2018) addressed the specific application of elastography-based methods in NAFLD, a condition of particular relevance given its rapidly rising prevalence in South Asia. They highlighted the advantages of vibration-controlled transient elastography and magnetic resonance elastography for risk stratification in NAFLD patients and called for clearer clinical guidance on how these tools should be integrated into patient management algorithms. The present study population included patients with NAFLD and MASLD among its enrolled cases, and the strong stiffness-fibrosis correlation observed across the cohort suggests that elastography performs reliably in this etiological subgroup as well.

The slight male predominance (57.3% males vs. 42.7% females) observed in this study is consistent with published data on the sex distribution of chronic liver disease in South Asian populations, where males demonstrate a higher overall burden of hepatitis B and C, alcohol-related liver disease, and advanced fibrosis. The bimodal distribution of fibrosis stages, with F2 and F4 predominating, is consistent with referral patterns typical of diagnostic centers where patients are evaluated when clinical signs of intermediate or advanced liver disease have prompted medical consultation.

The combined interpretation of grayscale ultrasound and elastography findings in this study reveals a clinically meaningful pattern: patients with coarser echotexture, irregular surface contour, increased portal vein diameter, and

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splenomegaly on grayscale imaging consistently demonstrated higher kPa values on elastography, corresponding to more advanced fibrosis stages. This convergence of morphological and biomechanical imaging data reinforces the value of using both modalities in tandem rather than relying on either alone. In clinical practice, a grayscale appearance suggestive of advanced fibrosis combined with high kPa values provides a more robust and clinically actionable diagnostic conclusion than either finding in isolation.

Comparison with Other Studies

The findings of the present study align closely with previously published international evidence on noninvasive liver fibrosis assessment. Soresi et al. (2014) conducted a comprehensive review of non-invasive tools for diagnosing liver cirrhosis and concluded that while ultrasound provides useful morphological information for advanced disease, elastography offers superior sensitivity for detecting earlier stages of significant fibrosis and provides a more reliable basis for staging. Their conclusion that combining imaging modalities and serum markers offers the best overall diagnostic accuracy is consistent with the integrated approach advocated by the present study.

Kemp and Roberts (2019) evaluated the feasibility and performance of the FibroScan XL probe in patients with elevated BMI and reported acceptable reliability of elastography measurements even in technically challenging cases. Jeong et al. (2014) outlined the principles and clinical applications of ultrasound elastography for diffuse liver disease and emphasized its role in differentiating mild from advanced fibrosis a distinction with direct implications for antiviral therapy initiation and surveillance scheduling.

Maurizio et al. (2014) specifically examined the reliability and diagnostic performance of transient elastography in chronic hepatitis C patients and reported a partial correlation coefficient of 0.71 between liver stiffness measurements and METAVIR histological staging, with ROC curve areas of 0.88 for significant fibrosis and 0.99 for cirrhosis. The Spearman correlation coefficient of 0.91 observed in the current study exceeds these values, potentially reflecting the broader inclusion of fibrosis stages and the use of a robust multicenter design. Cornberg et al. (2025), in the most recent EASL Clinical Practice Guidelines on hepatitis B management, incorporated liver stiffness measurement as a key component of non-invasive fibrosis assessment algorithms, recommending elastography as the preferred staging tool in the absence of confounding factors. The present study provides regionally relevant supporting data for these guideline recommendations within the South Asian hepatological context.

Limitations

Despite providing clinically meaningful and statistically robust insights, this study is subject to several limitations that should be carefully considered when interpreting and generalizing the findings. First, the cross-sectional study design employed in this investigation does not permit the establishment of causal or temporal relationships between liver stiffness measurements and fibrosis progression. Longitudinal data would be necessary to determine whether serial elastography measurements can reliably track disease progression or treatment-induced fibrosis regression over time.

Second, the study was conducted exclusively at selected diagnostic centers in Rahim Yar Khan, Pakistan, which may limit the generalizability of the findings to other geographic regions, ethnic populations, or healthcare settings with different patient demographics, disease etiologies, or referral patterns. A broader multicenter design spanning multiple cities or provinces would enhance the external validity of these results.

Third, while a sample of 110 patients provided adequate statistical power for the primary correlation and regression analyses, it may not be sufficient for robust subgroup analyses by etiology, gender, age, or comorbidity. Future studies with larger sample sizes would allow for more granular investigation of fibrosis predictors within specific clinical subgroups.

Fourth, direct histopathological confirmation through liver biopsy was not performed for all

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study participants. Fibrosis staging relied on established elastography cutoff values referenced against METAVIR criteria from the international literature, rather than tissue-based histological validation. While this approach is accepted in clinical practice and increasingly supported by guidelines, it introduces the potential for staging discordance compared to biopsy-confirmed assessments.

Fifth, although active hepatic inflammation, cholestasis, hepatic congestion, and elevated ALT all recognized confounders of liver stiffness measurements were incorporated as exclusion criteria, residual confounding from subclinical or undetected conditions cannot be entirely excluded. Future longitudinal, multicenter investigations with larger and more heterogeneous cohorts, direct histopathological correlation, and comprehensive multiparametric imaging analysis are strongly recommended to build on the findings of the present study.

5. CONCLUSION

This multicenter cross-sectional study of 110 patients with chronic liver disease, with an age range of 31 to 68 years, demonstrated a very strong and statistically highly significant positive correlation between liver stiffness measurements obtained by ultrasound elastography and METAVIR fibrosis staging. Spearman correlation analysis yielded $r_s = 0.91$ with $p < 0.005$, confirming that higher liver stiffness values are robustly and consistently associated with advancing fibrosis severity. Linear regression further validated liver stiffness as an exceptionally powerful independent predictor of fibrosis stage, with $\beta = 0.042$, $R^2 = 0.83$, and $p < 0.005$, establishing that 83% of the variation in fibrosis stage across the cohort was explicable by kPa measurements alone.

The progressive increase in mean liver stiffness values from 5.9 kPa in F0 to 58.3 kPa in F4, combined with the corresponding grayscale ultrasound findings of escalating hepatic echogenicity and echotexture coarsening, provides compelling evidence for the complementary diagnostic utility of both imaging modalities when used in an integrated approach. These findings confirm that ultrasound elastography is a reliable, reproducible, and clinically practical non-invasive tool for the accurate assessment and staging of hepatic fibrosis, capable of substantially reducing dependence on invasive liver biopsy in appropriately selected patients. Early non-invasive fibrosis detection through combined grayscale ultrasound and elastography assessment is strongly recommended for patients with suspected chronic liver disease, enabling timely clinical intervention and preventing progression to cirrhosis and its associated lifethreatening complications.

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DECLARATION

The authors declare that this article is original work and has not been submitted or published elsewhere.

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