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Liver Stiffness Distribution in Pakistani Adults Assessed by Ultrasound Sheer Wave Elastography: A Cross-Sectional Study

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ABSTRACT

Objective: To determine the normative percentiles for Liver Stiffness Measurement (LSM) using Shear Wave Elastography in an adult Pakistani population.

Methodology: This cross-sectional study was conducted at PESSI Hospital, Islamabad, from January to December 2023. Individuals aged 20 years and older, comprising both self-referred individuals, referral by plastic surgeon as part of holistic wellness evaluations in patients presenting for body contouring or reconstructive procedures, where liver ultrasound was recommended as a precautionary measure, seeking wellness evaluations and those referred for liver assessments by other medical specialties were included. Liver stiffness measurements (LSM) were obtained using 2D shear wave elastography, with image quality assessed and ten acquisitions recorded per subject. Only measurements with an interquartile range to median (IQR/M) ratio ≤30% were deemed reliable.

Results: Most liver assessments (87.69%) revealed a smooth surface. surface with small round bumps or lumps were observed in 5.00% and 4.61% of cases each, while micronodules were present in 4.61%. Irregular surfaces were absent in grade 1 livers but increased in prevalence with higher grades (1.00% in grade 2, 6% in grade 3, 26.24% in grade 4, and 22.68% in grade 5). Nodular surfaces were similarly absent in grades 1 and 2, but were found in 14% of grade 3 livers, 12.20% of grade 4 livers, and 25.46% of grade 5 livers. Micronodules were present in 1.00% of grade 1 and 2 livers and increased significantly in higher grades.

Conclusion: Real-time Shear Wave Elastography is a dependable method for assessing liver stiffness. In generally healthy adults, factors such as male sex, obesity, abnormal tummy shape and hepatic steatosis significantly influence liver stiffness levels.

Keywords: Liver / diagnostic imaging, Body Mass Index, Shear Wave Elastography, Liver Cirrhosis.

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Introduction

Liver diseases pose a significant health challenge in the Asia-Pacific region, contributing to 62.6% of global liver disease deaths, 54.3% deaths from cirrhosis, 72.7% of deaths from hepatoma, and acute viral hepatitis accounting for over two-thirds of the global burden, despite the region being home to more than half of the world's population.[1,2] Globally, nonalcoholic fatty liver disease (NAFLD) is a significant health concern, affecting an estimated 15% to 25% of the population.[3] In Asian countries, the prevalence of NAFLD is notably higher, ranging from 15% to 49.85%.[4] In Asian countries, the prevalence of NAFLD detected via ultrasonography increased from 18.9% in urban areas in 2007 to 32.0% in 2009, and from 8.7% in rural areas in 2010 to 30.7% in 2016.[5] Research studies have revealed varying prevalence rates of nonalcoholic fatty liver disease (NAFLD) across different Indian cities. Notably, Mumbai reported a 16.6% prevalence, Chennai showed a 32% prevalence, and Thiruvananthapuram exhibited the highest prevalence at 49.8%.[5-7] Elastography evaluates and displays the biomechanical characteristics of tissues, focusing on the elastic forces that resist shear deformation. Since alterations in tissue stiffness or elasticity often precede structural modifications, their assessment is crucial for early disease detection and tracking its progression, providing valuable predictive information.[8,9] By inducing dynamic stress, shear wave elastography (SWE) creates shear waves within tissues. This advanced imaging method enables evaluations of tissue elasticity both qualitatively and quantitatively. Young’s modulus (E) is used for the measurement of waves speed within the tissue and is expressed in meters per second (m/s) or kilopascals (kPa). SWE techniques are less operator-dependent, penetrate deeper, and are less prone to signal decay. Additionally, they present a more accessible, affordable, and a widely accessible substitute for computed tomography (CT) and magnetic resonance imaging (MRI) while delivering higher-quality images compared to conventional ultrasound.[10]

Early detection of chronic diseases, particularly metabolic disorders, is being facilitated in some Asian countries through preventive radiology programs that leverage imaging-based biomarkers.[11] This initiative focuses on evaluating endothelial dysfunction to inform treatment planning through the development of imaging protocols, and to assess the effectiveness of therapies on affected organs by monitoring disease progression and treatment-related changes in organ structure and function. With rising attention to self-image and aesthetics in today’s mobile-driven culture, more individuals are seeking body contouring procedures. Plastic surgeons now often recommend preoperative liver screening in such patients, especially those with obesity or abnormal abdominal shape, to ensure surgical safety and offer added preventive health benefits.

In Pakistan, normative age-specific percentiles adjusted for sex and body mass index (BMI) for liver stiffness measures derived from two-dimensional (2D) ultrasound SWE are currently unavailable.

Despite the growing use of SWE in clinical hepatology, there is a noticeable gap in the literature regarding normative LSM values in South Asian populations, particularly in Pakistan. Most existing reference ranges have been derived from Western or East Asian cohorts[5-7], which may not be generalizable due to genetic, environmental, dietary, and lifestyle differences that could influence liver stiffness. Moreover, there is a dearth of large-scale studies providing age, sex, and BMI-adjusted percentiles for SWE-derived LSM values in healthy individuals from Pakistan. This presents a significant limitation in the clinical application of SWE, as applying inappropriate reference ranges could lead to over- or underestimation of liver fibrosis, potentially affecting clinical decision-making.

This study aims to address this critical gap by providing robust, population-specific reference percentiles for LSM stratified by age, sex, and BMI in a healthy Pakistani cohort. By doing so, it will enable more accurate interpretation of liver stiffness in the Pakistani population and serve as a foundation for future research and clinical application in liver disease screening and monitoring.

Methodology

This was a cross-sectional study conducted at PESSI hospital Islamabad from January 2023 to December 2023 and consecutively recruited eligible participants from the radiology department. Individuals aged 20 years and older, comprising both self-referred individuals, those referred by plastic surgeons for preoperative evaluation in cases of obesity or abnormal abdominal shape, and those referred for liver assessments by other medical specialties, were included after providing informed consent.

Cases in which a reliable elastogram or an adequate acoustic window could not be achieved were excluded. The sample size was determined online using Raosoft software with a 50% anticipated NAFLD prevalence, a 5% absolute precision, a 95% confidence interval, with a projected response rate of 90% and a design effect of 2. Demographic and clinical information collected from all participants included occupation, age, height, weight, gender and a history of metabolic syndrome, HTN, DM, IHD, thyroid disorders, sleep apnea, daytime drowsiness, hepatitis and dyslipidemia for both genders. BMI was calculated for each individual, while medical records provided information on Hba1c, alanine transaminase (ALT), aspartate transaminase (AST) and blood sugar levels. Personal risk factors such as physical activity levels, alcohol and tobacco usage, unhealthy eating habits, and coffee intake were recorded based on self-reported data.

Liver stiffness grades are used to classify the severity of liver fibrosis, typically assessed by non-invasive elastography methods such as Shear Wave Elastography (SWE), Transient Elastography (TE, e.g., FibroScan), or Magnetic Resonance Elastography (MRE). These grades correlate with the histological stages of liver fibrosis, often based on scoring systems like METAVIR, Ishak, or Batts-Ludwig.

Table I: shows the classification of grades.

Fibrosis Grade	METAVIR Stage	Description	Typical Liver Stiffness (kPa)
F0	No fibrosis	Normal liver tissue	< 5.5 kPa
F1	Mild fibrosis	Fibrosis without septa	5.6 – 7.0 kPa
F2	Moderate fibrosis	Portal fibrosis with few septa	7.1 – 9.5 kPa
F3	Severe fibrosis	Numerous septa without cirrhosis	9.6 – 12.5 kPa
F4	Cirrhosis	Advanced fibrosis with nodular regeneration	> 12.5 kPa

Liver 2D SWE was performed by a radiologist who has a minimum of 20 years' experience in liver imaging. Participants were instructed to fast for a minimum of 4 hours prior to the procedure. The examination was carried out using an intercostal approach, with the patient lying in the left lateral position at 30 degrees and the right arm elevated above the head to widen the intercostal space, enabling the liver to be visualized in B-mode[12].

To ensure accurate liver stiffness measurements using Shear Wave Elastography (SWE), the B-mode ultrasound images were optimized to clearly visualize the liver capsule. The transducer was positioned perpendicularly to the liver surface to obtain the best acoustic window. A 2-3 cm ROI was placed 1-2 cm below the capsule, avoiding major and minor vessels. The STE ROI box was carefully positioned within a homogenous area of the liver parenchyma, excluding any anatomical structures. Patients held their breath at mid-expiration, and a series of STE images were captured over 3-5 seconds to create a cine loop.

The optimal STE image frame was selected based on the five green stars motion stability index (M-STB) and the reliability (RLB) map. A full green color indicated high shear wave quality, ensuring accurate and reproducible stiffness measurements. The M-STB index assesses motion interference, with fewer than four stars signaling significant interference, and more than four stars indicating minimal or no interference. These star ratings are color-coded as orange for low interference and green for high interference, facilitating easy interpretation. A stable SWE was identified when multiple consecutive frames displayed green stars on the M-STB. The RLB map, which reflects shear wave intensity, highlights reliable measurement areas in green and unreliable ones in purple. STE measurements were performed by avoiding purple-coded regions and ensuring a minimum of four green stars in the five-star stability index.

To ensure accurate and reliable SWE measurements, a 15 mm diameter "circle" was positioned within the ROI for consistent measurement within a homogeneous area. A single measurement was acquired per acquisition and reported as either shear wave speed (m/s) or stiffness (kPa). If artifacts were present, the "circle" diameter was reduced to 10 mm. Measurement variability was assessed by calculating the IQR/M ratio from ten acquisitions. High-quality measurements were defined as those with IQR/M ratios ≤30% for kPa and ≤15% for m/s.[12,14]

Measurements were excluded if they exhibited poor image quality, significant instability, unreliable indices, or fell outside of 3 standard deviations from the mean, indicating extreme values or outliers. Using a high-resolution linear probe, the liver surface was meticulously examined for irregularities, such as micronodules, which were defined as nodules measuring less than 2 mm. An irregular liver surface was characterized by disruptions in the smooth, echogenic contour, commonly presenting as uneven or wavy margins.

SPSS version 24 was employed for data analysis. Categorical data were presented as proportions, while continuous data were expressed as means with standard deviations (SD). For LSM percentiles, a subgroup of the study population without comorbidities was chosen. The normality of LSM was evaluated using the Shapiro-Wilk test, along with skewness and kurtosis analysis. The 10th, 25th, 50th, 75th, and 90th percentiles were calculated for each age group. To assess the effectiveness of the estimated percentiles, a threshold based on the 90th percentile of LSM was used to identify abnormal measurements. Sensitivity, specificity, PPV, and NPV were assessed using 2x2 table and formulas.

Results

A total of 260 individuals participated in the study, undergoing Shear Wave Elastography (SWE) between January 2023 and December 2023. The majority (80.00%) were referred for liver assessments by other medical specialties. Patient demographics and clinical characteristics are detailed in Table II.

Table II: Patient demographics and clinical characteristics.

Characteristics	N(%)
Mean age (years)	40.40±2.00
Gender	
Male	190 (73.07)
Female	70 (26.92)
BMI >32	110 (42.30)
DM	62 (23.84)
HTN	60 (23.07)
IHD	14 (5.38)
Abnormal Lipid Profile	128 (49.23)
Micronodules	12 (4.61)
Nodular Liver Surface	13 (5.00)
Irregular Liver Surface	12 (4.61)

The majority of liver assessments (87.69%) revealed a smooth surface. Irregular or nodular surfaces were found in 5.00% and 4.61% of cases, respectively, and micronodules were noted in 4.61% of cases. Irregular liver surfaces were not present in grade 1 livers but their frequency increased with higher grades (1.00% in grade 2, 6% in grade 3, 26.24% in grade 4, and 22.68% in grade 5). Nodular surfaces were similarly absent in grades 1 and 2, but were found in 14% of grade 3 livers, 12.20% of grade 4 livers, and 25.46% of grade 5 livers. Micronodules were present in 1.00% of grade 1 and 2 livers and increased significantly in higher grades (6% in grade 3, 28.60% in grade 4, and 32.44% in grade 5).

Based on liver stiffness measurements (LSM), 20.60% of individuals exhibited compensated advanced chronic liver disease (cACLD), while 5.24% displayed clinically significant portal hypertension (CSPH). In 21.64% of cases, LSM suggested cACLD, but further confirmatory tests were deemed necessary (Table III). A strong correlation was observed between LSM and liver fibrosis grades.

Table III: Dissemination of the grades of the liver fibrosis (based on liver stiffness measurements in shear wave elastography).

Characteristics	N%	Interpretation
< 5kpa	5.08	High probability of being normal
< 9kpa	54.87	In the absence of other clinical signs, rules out cACLD. Needs further tests based on clinical signs.
9-13kpa	21.64%	Indicative of cACLD but needs further valuation
>13kpa	20.60%	Management in cACLD
>17kpa	5.24%	Indicative of CSPH

Using a generalized least squares multivariable fractional polynomial regression model, the 10th, 25th, 50th, 75th, and 90th percentiles of LSM by age groups were calculated, with adjustments made for sex and BMI.

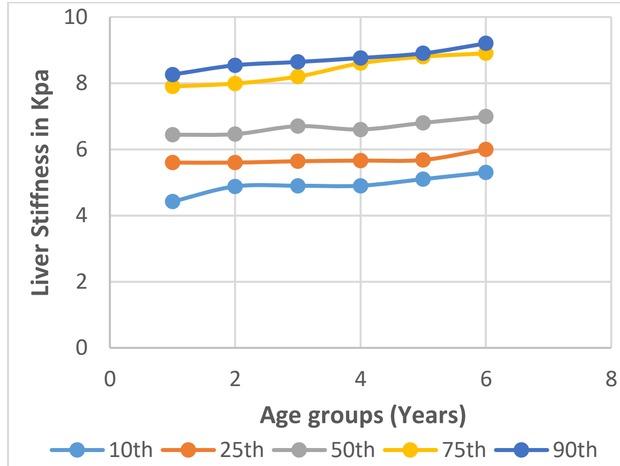

Figure 1: Liver stiffness measurement centiles by age, adjusted for sex and body mass index (BMI), in an adult Pakistani population.

Compared to the LSM category exceeding the 90th percentile, AST and ALT demonstrated suboptimal effectiveness in identifying liver changes suggestive of cACLD, confirming cACLD diagnoses and identifying CSPH. The results are shown in table III.

Table IV highlights the superior diagnostic accuracy of Shear Wave Elastography (SWE) in predicting clinically significant portal hypertension, with a sensitivity of 91.0% and specificity of 94.8%, outperforming ALT and AST levels.

Table IV: Evaluating the Effectiveness of Estimated 90th Percentile Liver Stiffness Measurements Obtained with Shear Wave Elastography in Predicting Clinically Significant Portal Hypertension, Alongside AST and ALT Levels.

Characteristics	90th percentile cutoff LSM value	ALT value	AST value
Specificity	94.8%	70.8%	80.4%
Sensitivity	91.0%	47.4%	53.3%
PPV	89.0%	23.2%	24.9%
NPV	93.2%	80.4%	82.45
PLR	22.6	1.00	1.23
NLR	1.0	0.72	0.89
AUROC	0.80	0.48	0.90
Diagnostic Odds ratio	244.0	1.54	1.87

Discussion

This study identified male gender, increased body weight, and the presence of hepatic steatosis as key determinants of liver stiffness among healthy adults. The mean liver stiffness observed in our sample was 4.90 ± 0.64 kPa, which is in agreement with previously published data—5.1 kPa in China, 4.5 kPa in Norway, and 5.1 kPa in Albania[14]—further validating the consistency of our findings across diverse populations.[16] Our study examined the impact of key variables—age, gender, BMI, and hepatic steatosis—on shear wave elastography (SWE) measurements. We found no statistically significant effect of age on liver stiffness, which is consistent with earlier research by Mulabecirovic et al.[15], Huang et al.[11], Suh et al.[8], and Arda et al.[17]

However, SWE values were significantly elevated in obese individuals compared to those with normal or overweight BMI categories ($p < 0.001$). While the influence of BMI on liver stiffness remains controversial, our findings align with a study conducted in the Egyptian population, which reported significantly increased liver stiffness measurements in individuals with BMI ≥ 26 kg/m².[18] Given this association between obesity and increased liver stiffness, plastic surgeons—particularly those evaluating patients for abdominoplasty or body contouring—can contribute by recommending liver screening as part of preoperative workup. This not only improves surgical safety but also offers patients a valuable preventive obesity related health advantage.

Previous studies by Mulabecirovic et al.[15] and Huang et al.[11] did not observe a significant association between BMI and liver stiffness, but it's important to note that these studies excluded subjects with obesity (BMI > 30 kg/m²). Therefore, the absence of obese participants may explain the differing outcomes, further supporting the relevance of our findings.

The present study showed that males had higher average SWE measurements than females, with the difference reaching statistical significance. This trend aligns with findings from studies carried out in Norway[15] and China[14]. In contrast, investigations from India[17] and Egypt[18] did not observe any significant sex-based variation in SWE values. In our study, SWE values did not differ significantly among underweight, normal-weight, and overweight groups. However, obese individuals (BMI > 30 kg/m²) exhibited notably higher liver stiffness measurements compared to the other categories. The effect of BMI on liver stiffness is debated in current literature. A study involving the Albanian population reported no statistically significant difference in LSM values between subjects with BMI above and below 30 kg/m².

Consistent with this, studies by Mulabecirovic et al.[15] and Huang et al.[11] also found no BMI-related differences in liver stiffness, although their analyses were limited to non-obese individuals. The exclusion of obese participants likely contributed to the lack of observed significance, mirroring our findings within similar BMI categories. In contrast, an Egyptian study[18] reported significantly elevated LSM values in individuals with BMI ≥ 26 kg/m², highlighting potential variability across populations.

We observed a clear association between hepatic steatosis and increased SWE values in our cohort. However, this contrasts with the findings of Suh et al.[8], who reported no significant difference in liver stiffness between steatotic and non-steatotic groups. A likely explanation for this variation is that the majority of subjects in their study (65 out of 71) had only low-grade (Grade 1) steatosis, which may have limited the ability to detect meaningful changes in liver elasticity.

In our study, only five subjects with normal clinical and sonographic findings underwent liver biopsy, which confirmed the absence of fibrosis. These individuals were potential liver transplant donors. Given the scarcity of healthy adults subjected to invasive biopsy procedures in our context, obtaining histopathological confirmation to exclude hepatic fibrosis was limited.

Liver elastography has long been employed to measure liver stiffness and offers a promising, non-invasive alternative to biopsy and histopathology. While previous research has defined normal liver stiffness ranges in healthy subjects, this study is the first to provide such data specifically for healthy Pakistani adults, establishing essential reference values and detection criteria for the local population and future studies.

Conclusion

To conclude, this study successfully establishes sex-, age, and BMI-adjusted reference percentiles for liver stiffness measurements (LSM) using shear wave elastography in a healthy adult Pakistani population. These normative values fill a critical gap in the literature by providing population-specific benchmarks that can enhance the interpretation of LSM results. The findings lay a foundational framework for future clinical, plastic surgical and epidemiological studies aimed at identifying and stratifying liver fibrosis in this region. Ultimately, this work has the potential to support the development of more accurate, long term follow up post operatively, locally relevant diagnostic and prognostic tools for liver disease assessment in Pakistani and similar South Asian populations.

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