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# Estimation of Hepatic Elasticity by Shear Wave Sonoelastography among Asymptomatic Individuals in a Tertiary Level Hospital

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## ABSTRACT

**Background:** Shear wave elastography is currently most widely used method for determining the elasticity of liver. Liver fibrosis, final common pathway of chronic liver disease, is associated with increased liver stiffness. This study aimed to obtain normal liver elasticity in Nepalese population, as it can be used as reference in future for determination of elasticity in abnormal liver.

**Methods:** Quantitative prospective study was done in 132 individuals with normal liver function tests. Shear wave elastography was done to measure elasticity of both lobes of liver and thus obtained values were also correlated with age, gender and fatty changes in liver.

**Results:** Forty seven out of 132 individuals had fatty liver. Mean elasticity of liver was 4.40±0.60 kPa with range of 3.12-6.62 kPa. There was no significant difference between mean elasticity of right and left lobe of liver. No significant correlation was found between mean liver elasticity with age and gender. There was statistically significant difference in the mean elasticity between non-fatty and fatty liver ($p=0.041$).

**Conclusions:** The study established normal elasticity of liver in Nepalese population and this reference can be used to obtain abnormal liver elasticities.

**Keywords:** Elasticity; normal liver; shear wave

## INTRODUCTION

Common final pathway of chronic liver disease is progressive fibrosis. Assessment of liver fibrosis is important not only for follow up of chronic liver disease, but also for its management and prognostic evaluation.[1] Although biopsy is gold standard for estimation of liver fibrosis, reproducible non-invasive modalities are important for monitoring of the disease and response evaluation following treatment.[2]

Sonoelastography, a non-invasive technique for liver fibrosis assessment, has been widely developed in clinical practice. The shear wave elastography is currently most widely used method for determining the elasticity of liver.[3]

Normal reference values of the liver elasticity should be available before determining the abnormal liver elasticity. Till date no studies have been done in Nepal about normal liver elasticity estimation. This study was done to obtain normal liver elasticity in healthy Nepalese individuals, so that the results of this study can be used in future for determination of abnormal liver stiffness or liver fibrosis.

## METHODS

Hospital based quantitative cross-sectional study was done in Ultrasound unit of Department of Radiology and Imaging, Tribhuvan University Teaching Hospital during a period of October 2014 to September 2015. Point Shear Wave Elastography was performed in the individuals with Phillips-iU-22 (C 1-5 MHz probe) Ultrasonography (USG) unit within the department.

Approval of ethical clearance was obtained from Institutional Review Board, Institute of Medicine. The individuals were explained about the study and were included in the study after obtaining the written

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informed consent. No active intervention was done in any individuals involved in the study.

Individuals in the age group of 15 – 60 years and normal liver function tests were included in the study. Any individuals with features of acute or chronic liver disease, any systemic disease that may affect liver, any focal hepatic lesions or any history of hepatic surgery were excluded from the study.

Individuals who met the inclusion criteria (n= 132) underwent USG of abdomen. Size of liver was measured in anteroposterior direction in mid-clavicular line as suggested by Gosink et al.[4] Fatty changes in liver, if present was noted and graded into Grade I-III.[5] Shear wave elastography of liver was then performed. Elasticity was measured in segment V and VI of right lobe of liver and segment III or IVb of left lobe of liver. Elastography region of interest box was set to area of 1 cm x0.5 cm in the target area. To avoid erroneous measurements, care was taken to put the ROI box at vessel-free region of liver parenchyma with the upper edge of the ROI box at least 2 cm below the liver capsule. For each subject, three consecutive elasticity measurements were obtained by using similar technique for both lobes of liver. Each measurement was obtained during a separate breath hold. Median of three elasticity measurements were taken for right and left lobes of liver and expressed in kilopascals. Median of thus obtained elasticity of right and left lobes of liver were taken as the representative measurement of the liver elasticity.[2]

Data obtained were compiled and analyzed using standard statistical analysis. SPSS 21 and Microsoft Excel were utilized for the data analysis and presentation. Pearson's correlation was used to determine the correlation of age, BMI and size of liver with mean liver elasticity. Student t-test was used to determine the relation of gender with liver elasticity. Various graphs were also derived from the study using these softwares.

## RESULTS

Total of 132 individuals (68 male and 64 female) were included in the study. Mean age was 38.7 years and maximum individuals (36) were in the age group of 21-30 years.

Mean anteroposterior size of right lobe of liver was 13.9±1.06cm. Among the 132 individuals, 47 had fatty liver, including Grade I fatty liver in 27 individuals, Grade II fatty liver in 16 individuals and Grade III fatty liver in four individuals.

Mean elasticity of liver was 4.40±0.60 kPa (shear wave velocity of 1.209±0.083 m/s) and median elasticity value was 4.41 kPa with interquartile range of 0.929 kPa (Table 1, Figure 1). There was no statistically significant difference in mean elasticity values of liver with respect to the gender (Table 2). No significant correlation was found between mean right lobe, left lobe and mean liver elasticity with age (Table 3, 4; Figure 2). There was statistically significant difference in the mean elasticity values between non-fatty and fatty liver (p=0.041) (Table 5). There was no significant difference between mean elasticity value of right and left lobe of liver (p=0.283) (Table 6).

Table 1. Mean values of liver elasticity and shear wave velocity in right and left lobe of liver (n=132)

| | Elasticity values (kPa) | Shear wave velocity (m/s) | SD (kPa) |
|---|---|---|---|
| Right lobe (minimum) | 2.94 | 0.99 | -- |
| Right lobe (maximum) | 6.4 | 1.46 | -- |
| Left lobe (minimum) | 2.71 | 0.95 | -- |
| Left lobe (maximum) | 7.09 | 1.54 | -- |
| Right lobe (mean) | 4.36 | 1.20 | 0.74 |
| Left lobe (mean) | 4.45 | 1.21 | 0.82 |
| Mean liver elasticity | 4.4 | 1.209 | 0.60 |

Table 2. Liver size and elasticity according to gender

| | Male | Female | p - value |
|---|---|---|---|
| Size of right lobe of liver (cm) | 14.2 (0.90) | 13.5 (1.1) | <0.01* |
| Mean elasticity (kPa) of right lobe (SD) | 4.41 (0.70) | 4.31 (0.78) | 0.411 |
| Mean Shear wave velocity (m/s) of right lobe (SD) | 1.209 (0.09) | 1.193 (0.1) | |
| Mean elasticity (kPa) of left lobe (SD) | 4.56 (0.71) | 4.33 (0.9) | 0.098 |
| Mean Shear wave velocity of left lobe (SD) | 1.23 (0.09) | 1.195 (0.22) | |
| Mean elasticity (kPa) of liver (SD) | 4.49 (0.57) | 4.31 (0.62) | 0.103 |
| Mean Shear wave velocity (m/s) of liver (SD) | 1.221 (0.070 | 1.19 (0.08) | |

Table 3. Variation of BMI, liver size, elasticity according to different age groups of study population.

| Age (years) | <20 | 21-30 | 31-40 | 41-50 | 51-60 |
|---|---|---|---|---|---|
| Mean BMI (kg/m$^2$) | 21.3 (2.2) | 22.4 (2.2) | 23.2 (1.86) | 24.6 (1.95) | 24.6 (1.9) |
| Mean size (cm) of liver | 13.3 (1.1) | 13.6 (1.07) | 13.9 (1.09) | 14.0 (1.0) | 14.1 (0.9) |
| Mean elasticity (kPa) of right lobe | 4.4 (0.64) | 4.1 (0.71) | 4.6 (0.85) | 4.4 (0.63) | 4.2 (0.73) |
| Mean elasticity (kPa) of left lobe | 4.22 (0.73) | 4.2 (0.72) | 4.6 (0.87) | 4.5 (0.65) | 4.4 (0.95) |
| Mean elasticity (kPa) of liver | 4.33 (0.45) | 4.2 (0.60) | 4.6 (0.67) | 4.4 (0.48) | 4.3 (0.6) |
| Mean shear wave velocity of liver (m/s) | 1.20 (0.06) | 1.18 (0.08) | 1.24 (0.089) | 1.21 (0.06) | 1.20 (0.08) |

Table 4. Correlations of liver elasticity with age.

| Elasticity (kPa) | 'r' value ('p' value) |
|---|---|
| Mean right lobe elasticity | +0.001 (0.992) |
| Mean left lobe elasticity | +0.05 (0.569) |
| Mean liver elasticity | +0.033 (0.705) |

Table 5. Variation of elasticity according to grades of fatty liver.

| | Non-fatty liver | Grade I | Grade II | Grade III | p-value (ANNOVA) |
|---|---|---|---|---|---|
| Mean elasticity of right lobe (kPa) | 4.31 (0.72) | 4.43 (0.7) | 4.64 (0.7) | 3.62 (0.7) | 0.08 |
| Mean elasticity of left lobe (kPa) | 4.33 (0.74) | 4.71 (0.9) | 4.61 (0.9) | 4.57 (0.6) | 0.161 |
| Mean elasticity of liver (kPa) | 4.32 (0.58) | 4.57 (0.5) | 4.63 (0.7) | 4.09 (0.6) | 0.08 |
| Mean shear wave velocity of liver (m/s$^2$) | 1.19 (0.08) | 1.23 (0.06) | 1.23 (0.09) | 1.16 (0.08) | |

Table 6. Comparison of elasticity of right and left lobe of liver.

| | Mean (SD) | 'p' value |
|---|---|---|
| Right lobe elasticity (kPa) | 4.361 (0.74) | 0.283 |
| Left lobe elasticity (kPa) | 4.45 (0.81) | |

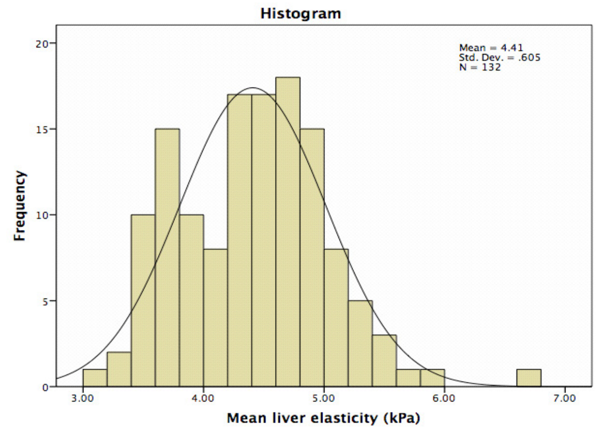


Figure 1. Histogram showing distribution curve of mean liver elasticity (kilopascals).

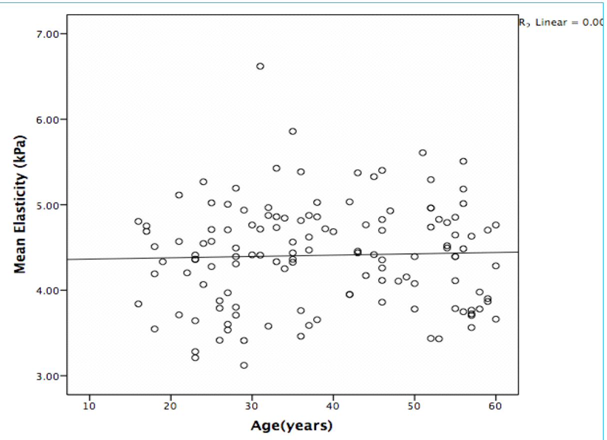


Figure 2. Scatter diagram-showing correlation of mean liver elasticity with age.

## DISCUSSION

Shear wave elastography of liver provides important information regarding the stiffness of the liver parenchyma. With increasing severity of hepatic fibrosis, parenchymal elasticity decreases and hence there is alteration of shear wave velocity (m/s) and Young's modulus (kPa), which can be easily estimated by means of ultrasound elastography. Many studies have shown that the Young's modulus (kPa) and shear wave velocity increases with increase in the severity of the hepatic fibrosis. Being a non-invasive method, ultrasound elastography is gaining popularity recently. In near future, researchers are hoping that this technology will be able to replace liver biopsy for diagnosis and grading severity of hepatic fibrosis.[3, 6, 7]

Mean elasticity of liver in our study was 4.40±0.60 kPa with range of 3.12-6.62 kPa. These elasticity values were comparable to earlier studies done by Suh et al,[2] Cha et al,[8] Sirli et al[9] and Huang et al.[10] Small variations observed as compared to other studies were likely due to variations in elastography techniques in different studies. Studies have shown that different techniques of elastography may alter the elasticity values.[7] Different techniques of elastography in clinical practice are strain elastography (SE), transient elastography (TE), acoustic radiation force impulse imaging (ARFI) and shear wave elastography (SWE).[11]

Confounding factors age and gender showed negligible effects on liver elasticity in our study, which is in agreement with similar studies conducted by Suh et al.[2] Liver elasticity was comparable in different age groups in study conducted by Ling et al[12] as well, however, in their study liver elasticity was higher in men (3.8 ± 0.7 kPa) than in women (3.5 ± 0.4 kPa) (p = 0.016). Sirli et al[9] also found higher elasticity in men (6.6± 1.5 kPa vs 5.7± 1.3 kPa), (p =0.01). The lower elasticity value in female is thought to be associated with the fact that the ovarian hormones inhibited the production of extracellular matrix by liver satellite cells, which make the liver softer.[13]

Although mean elasticity of individuals with fatty liver was significantly higher than that of non-fatty liver (p=0.041), there was no statistically significant difference in mean elasticity values with varying grades of fatty liver in our study (p=0.08). This difference might be because of lesser number of individuals with higher grade fatty liver (grade II and III) in our study. Also, non-alcoholic fatty liver disease (NAFLD) was not thought of in our study. Colombo et al[14] also found significant lower liver stiffness in individuals without fatty liver than those with fatty liver (p<0.001), however, Suh et al[2] found no statistical difference in elasticity between fatty and non-fatty liver (p=0.694). Suh et al correlated the elastography findings with liver biopsy finding, thus, it might be more reliable than our study.

Smaller sample size and non-availability of liver biopsy for corroborating our results are limitations of this study. Also, we took only two ROI in each subject, thus whole liver elasticity might not be represented in the results of our study. NAFLD was also not considered in our study. Thus, larger population based study including NAFLD patients and taking more ROI in both lobes of liver along with biopsy correlation needs to be conducted in our country as well to determine the variation of elasticity between fatty and non-fatty livers.

## CONCLUSIONS

This study established the normal values of hepatic elasticity in Nepalese individuals. No significant correlation of hepatic elasticity with age, sex and lobes were seen, however significant correlation with fatty liver was seen. Further large-scale studies representing more segments of liver and if possible, correlating with liver biopsy are necessary to determine variation of elasticity between fatty and non-fatty livers.

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