ORIGINAL ARTICLES

Normal Liver Stiffness Values in Adult Subjects by Magnetic Resonance Elastography

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Abstract

Background: *Chronic liver disease resulting in fibrosis, and ultimately cirrhosis, is a significant cause of morbidity and mortality worldwide. Conventional imaging techniques such as fibroscan and sono-elastography cannot detect early fibrosis or assess its grade to the histopathologic scale. Liver biopsy, despite being gold standard for detection of liver fibrosis, has limitations and is not well accepted by patients for its invasive nature and potential complications. Magnetic Resonance Elastography (MRE) is a well-established non-invasive newer imaging modality for determining liver stiffness and in most of the cases it can be an alternative to liver biopsy. A comprehensive knowledge of normal liver stiffness is necessary for the early detection of liver fibrosis.* ***Objective:*** *To determine normal liver stiffness values in adult subjects.* ***Materials and methods:*** *The cross-sectional study was carried out in the Department of Radiology and Imaging, BIRDEM General Hospital, Dhaka from October 2021 to September 2023. A total of 60 adult subjects were included in this study according to inclusion and exclusion criteria. Liver stiffness of the selected subjects was measured by MR elastography with a 1.5T MRI scanner through color mapping. The association of liver stiffness with age, sex and BMI of the subjects has also been described.*

Results: *Majority of the subjects belonged to the age-group 30-39 years and were predominantly female. Mean stiffness of the subjects was 2.42±0.20 kPa, with a range of 1.72-2.92 kPa. Mean stiffness for males and females were 2.46±0.19 kPa and 2.40±0.21 kPa respectively. Gender, age, and BMI did not exhibit any significant correlation with mean liver stiffness (p>0.05).* ***Conclusion:*** *The study determined normal liver stiffness values in adult subjects and stiffness did not have a statistically significant correlation with age, sex or BMI.*

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Introduction

Chronic liver disease (CLD) is a significant health issue in modern world including that in Bangladesh. In majority of the cases, it progresses from the stage of fibrosis to liver cirrhosis, ultimately leading to hepatocellular carcinoma and hepatic failure. Hepatitis B and C virus infections, long-term alcohol misuse, non- alcoholic fatty liver disease, metabolic and autoimmune liver disorders are risk factors for the development of cirrhosis. The incidence of fatalities from cirrhosis and its complications is still significant, even with the development of new therapies for some chronic liver diseases, such as hepatitis C.[11] Recent research has manifested that some stages of fibrosis may be reversible, which makes early detection and quantitative assessment of fibrosis necessary for intervention and treatment.[4] Hence, it is required to have a reliable, sensitive, and repeatable tool that allows a frequent and safe assessment of liver fibrosis. Available diagnostic imaging and laboratory procedures are able to diagnose CLD, but their performance in detecting

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and assessing earlier stages of fibrosis is not up to the level.[11]

Liver biopsy is gold standard for the assessment of liver fibrosis. However, because of its invasiveness and potential complications, it is limitedly used to monitor the fibrotic process.[11] It also has a procedure-related mortality rate of one in 10,000–12,000 patients. In addition, because of the small sample volume and sampling variability as well as the inter-observer variation in the interpretation of the semi-quantitative fibrosis scores, the assessment of liver fibrosis using a liver biopsy specimen may be questioned.[6] Thus, there has been an arising need for the development of a reliable, noninvasive method that could alternatively be used for assessment of stages of fibrosis.

Magnetic resonance elastography (MRE) is a dynamically developing noninvasive modality that allows assessment of stages of liver fibrosisa.[11]

MRE has also been found more accurate comparing to other non-invasive imaging modalities like sono- elastography and transient elastography in detection of liver fibrosis.[5-]

[18] MRE facilitates a quantitative evaluation of the mechanical characteristics of tissues by mechanical wave propagation analysis. The images, which are automatically processed to produce quantitative tissue stiffness maps known as elastograms, illustrate how the produced low-frequency shear waves (60 Hz) propagate through the liver tissue.[11]

Chronic liver disease causes progressive fibrosis of the organ, which increases its stiffness. The stiffness measurement closely parallels the progression of the fibrotic process. MRE is a safe, non-invasive, and reliable diagnostic imaging technique that has been shown in numerous trials to be effective in identifying the degree of liver damage in CLD patients. However, a credible assessment of an elastogram in a sick person is possible only by referring to normal liver stiffness values obtained by elastography in healthy subjects.[11]

To the best of our knowledge no prior study has been done in Bangladesh yet regarding this type of study. Therefore, the goal of this study was to detect the normal liver stiffness values in adult subjects and address its association with age, sex and body mass index (BMI).

Materials and Methods:

This cross-sectional study was performed in the Department of Radiology and Imaging, BIRDEM General Hospital, Dhaka from October 2021 to September 2023. A total of 60 adult subjects referred to the Department of Radiology and Imaging at BIRDEM General Hospital for MRI of whole abdomen and MRCP with no self or family history of liver disease, BMI within normal range, normal liver function test, screening-test-negative for liver disease and no abnormal liver parenchyma at ultrasonography were included in the study. Subjects with pre- existing diabetes or hypertension, and with a history hepatotoxic drug intake, alcohol abuse, claustrophobia and MR incompatible implants were excluded.

A whole-body MR scanner (PHILIPS Ingenia 1.5T) was used to perform the MRE scans. The study was performed after 4-6 hours of fasting with subjects in a supine position. In this study, the passive driver of MRI scanner was placed on the upper abdomen overlying the right lobe of the liver, with the center of the driver at the level of xiphisternum. An elastic abdominal binder strap was used to secure the passive driver. The passive driver was positioned with the largest of the liver right beneath it. Pressure pulses with a frequency of 60 Hz were produced by active driver unit and conveyed to the passive driver through flexible tubing. Slices of liver's largest cross section were obtained by acquiring axial MRE slices and planning them on the axial and coronal scout and T2-weighted images. All sequences were obtained during end-expiration and breath-hold for homogeneity. No intravenous contrast was applied during the process.

The scanner automatically processed the generated wave images, producing quantitative images that showed tissue stiffness (elastogram) using a 2D direct inversion algorithm supplied by the manufacturer. By positioning the regions of interest (ROIs) on the magnitude stiffness maps at four anatomically distinct liver slices, liver stiffness was determined. In each slice, four ROIs were carefully generated, either round or oval, avoiding areas of poor signal, fissures, motion artifacts, liver edges, the gallbladder, and major vessels. The liver edges were avoided to minimize edge artifacts, major vessels and fissures as they do not contain liver parenchyma.

Thus, the MRE software recorded the average stiffness me

The cross-sectional study was conducted in the Department of Radiology and Imaging at BIRDEM General Hospital, Dhaka. A total of 60 adult subjects who fulfilled inclusion and exclusion criteria were enrolled in this study from the patients referred for MRI of whole abdomen and MRCP.

The enrolled subjects underwent liver stiffness measurement by MRE with a 1.5T MRI scanner. The findings derived from the data analysis are furnished below:

Table-I

Distribution of the subjects by age (n=60)

Age group (years)	Number of subjects	Percentage (%)
20-29	13	21.7
30-39	33	55.0
40-49	10	16.6
50-55	4	6.7
Total	60	100.0
Mean±SD	35.5±8.15	
Range (min-max)	(20-55)	

Table I shows that the majority (55%) of subjects belonged to the age group 30 to 39 years. The mean age was 35.5±8.15 years with an age range from 20 to 55 years.

Figure-1 reveals that 68.3% of the subjects were female while 31.7% were male. Male to female ratio in the study was 1:2.2.

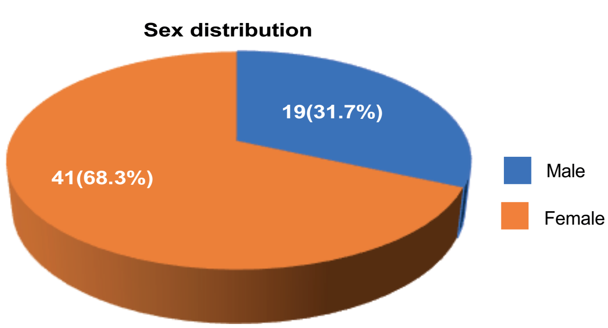


Figure 1: *Distribution of the subjects according to sex (n=60)*

Table-II

Distribution of BMI of the study subjects (n=60)

Descriptive Statistics	BMI (kg/m^2)
n	60
Minimum	18.6
Maximum	24.1
Mean	21.9
Std.Deviation	1.25

Table-II shows that BMI have had a mean of 21.9±1.25 kg/m^2, ranging from 18.6 to 24.1 kg/m^2.

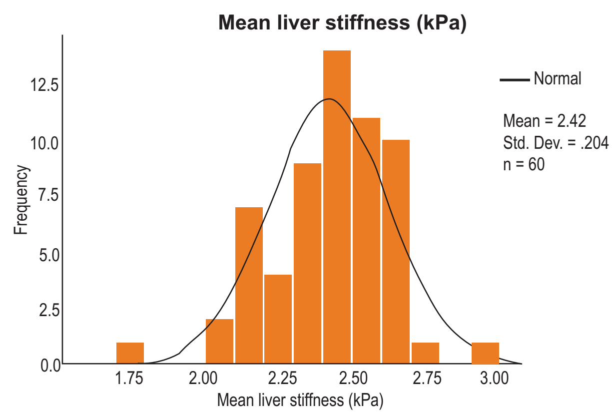


Figure 2: *Distribution of mean liver stiffness of study subjects*

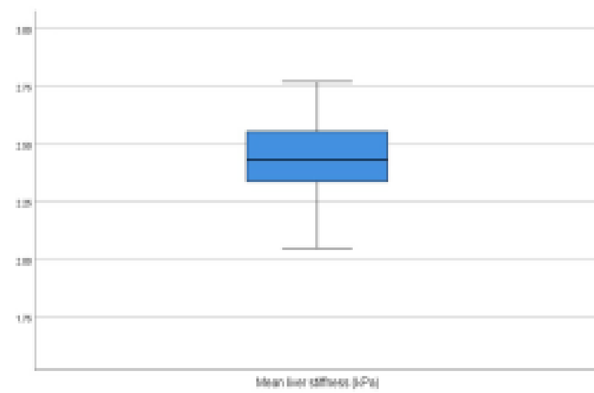


Figure 3: *Central tendency of mean liver stiffness of study subjects*

Table III

Central tendency of mean liver stiffness of study subjects

Descriptive Statistics	Mean liver stiffness
n	6
Minimum	1.72
Maximum	2.92
Mean	2.42
Std.Deviation	0.20

Central tendency of mean liver stiffness in the study subjects is showed in Figure-2 and Figure-3. The data represented in descriptive statistics is based on measurements obtained from 60 adult subjects. The 'Mean liver stiffness' refers to the average liver stiffness value calculated from the study sample. The values range from a minimum of 1.72 kPa to a maximum of 2.92 kPa, with a mean of 2.42±0.20 kPa. The range of stiffness values suggests variability among individuals, with some subjects having lower stiffness values and others having higher stiffness values. The relatively small standard deviation (0.20) around the mean indicates that the data points are clustered close to the average, implying a certain level of consistency in liver stiffness measurements amongst the adult subjects enrolled in the study.

Table-III

Comparison of mean liver stiffness among different age groups (n=60)

Age group (years)	n	Liver stiffness (kPa)		*p*-value
		Mean±SD	Range (min-max)	
20-29	13	2.45±0.12	2.15 – 2.61	
30-39	33	2.40±0.21	2.05 – 2.92	
40-49	10	2.38±0.29	1.72 – 2.77	0.305
50-55	4	2.59±0.08	2.50 – 2.67	
Total	60	2.42±0.20	1.72 – 2.92	

Table-III shows a comparison of liver stiffness among different age groups (20-29, 30-39, 40-49, and 50-55 years). The mean stiffness values (mean±SD) for different age groups were as follows: 2.45±0.12 kPa for the 20-29 age group, 2.40±0.21 kPa for the 30-39 age group, 2.38±0.29 kPa for the 40-49 age group, and 2.59±0.08 kPa for the 50-55 age group. The mean stiffness for all age-groups was 2.42±0.20 kPa. There is no statistically significant difference in liver stiffness amongst the age groups in this study (p>0.05).

Table-IV

Comparison of mean liver stiffness between male and female (n=60)

Gender	n	Mean±SD	Range (min-max)	*p*-value
Male	19	2.46±0.19	2.15 – 2.92	
Female	41	2.40±0.21	1.72 – 2.66	0.272
Total	60	2.42±0.20	1.72 – 2.92	

p-value obtained by Unpaired t-test, p< 0.05 considered as a level of significance.

Table-IV shows the mean stiffness values for male and female subjects were 2.46±0.19 kPa and 2.40±0.21 kPa respectively. The overall mean stiffness for all subjects combined was 2.42±0.20 kPa. The findings suggest that there is no significant variation in liver stiffness between males and females (p>0.05). This implies that gender does not appear to be a significant factor influencing liver stiffness in this particular population.

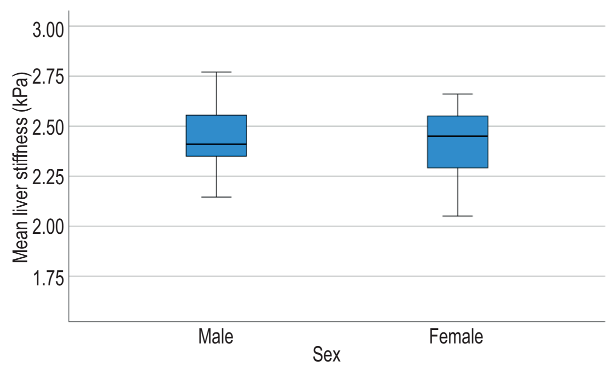


Figure 4: *Central tendency of mean liver stiffness in male and female subjects*

Table-V

Correlation of mean liver stiffness with age and BMI (n=60)

	Pearson correlation	
	r-value	p-value
Stiffness vs age	0.061	0.645
Stiffness vs BMI	-0.036	0.782

Table-V reflects the correlation of mean liver stiffness with age and BMI in the study subjects (n=60) using Pearson correlation analysis. The correlation coefficient between stiffness and age was 0.061, with a p-value of 0.645 which indicates a weak positive correlation that was not statistically significant. Similarly, there was no significant correlation between mean liver stiffness and BMI, with a correlation coefficient of -0.036 and a p-value of 0.782. These results suggest that mean liver stiffness is not significantly associated with age or BMI (p>0.05).

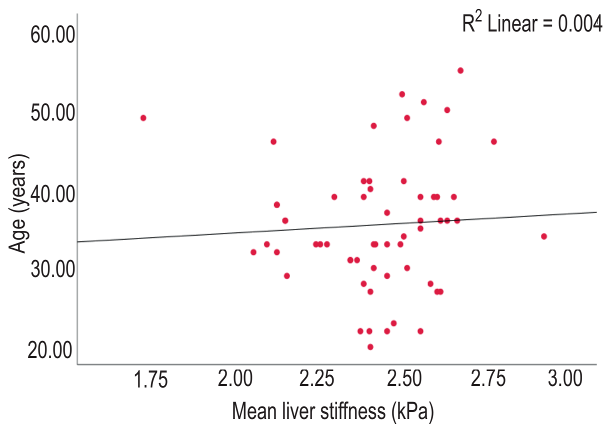


Figure 5: *Scatter diagram showing the correlation of mean liver stiffness with age*

Figure-5 shows the correlation between mean liver stiffness of the study subjects with age. Pearson Correlation analysis revealed that the mean liver stiffness did not show a significant correlation with age (r = 0.061, p = 0.645) suggesting that age may not be a determining factor for liver stiffness in this study group.

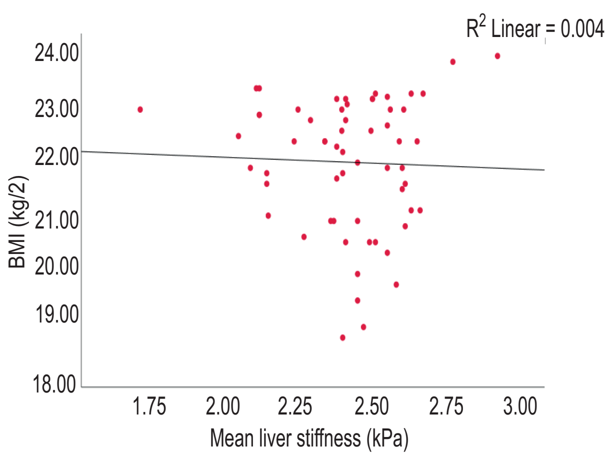
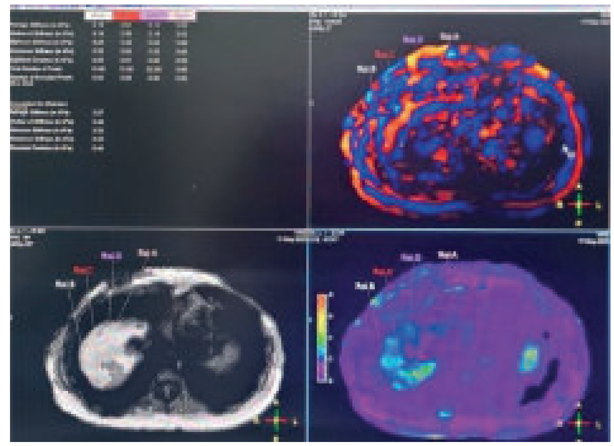
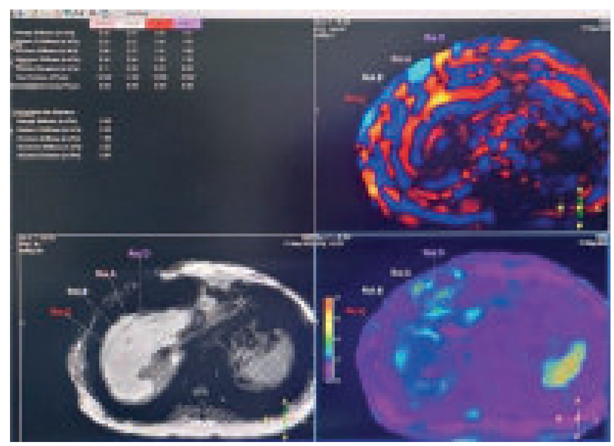


Figure 6: *Scatter diagram showing the correlation of mean liver stiffness with BMI*

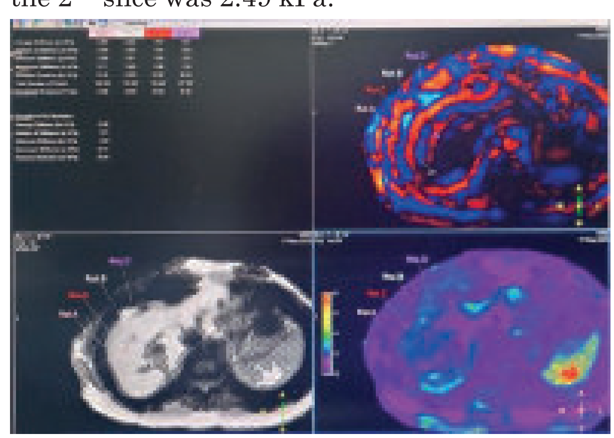
Figure 6 represents the correlation of mean liver stiffness with BMI in the study subjects using Pearson Correlation Analysis. The correlation co-efficient between stiffness and BMI indicates a weak negative correlation. These results indicate that liver stiffness is significantly associated with BMI (r=-0.036, p = 0.782).



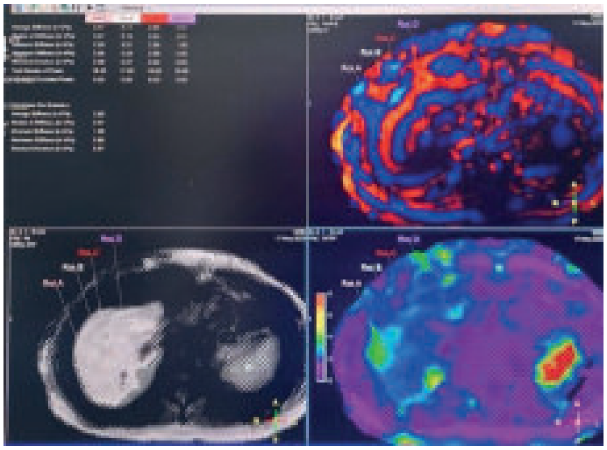
Photograph-1: MRE of liver of a 27 years old female showing axial magnitude image, wave image, and stiffness map from the MRE sequences (1st slice.) Four ROIs placed in the liver avoiding liver edge, vessels, and any areas of wave interferences. The average liver stiffness from this slice was 2.57 kPa.



Photograph-2: The average liver stiffness from the 2nd slice was 2.49 kPa.



Photograph-3: The average liver stiffness from the 3rd slice was 2.28 kPa.



Photograph-4: The average liver stiffness from the 4th slice was 2.83 kPa. The mean liver stiffness for four slices was 2.54 kPa.

Discussion

In this study, we observed that majority of the subjects (55%) belonged to the age-group 30-39 years. The mean age was

35.5±8.15 years comprising age range of 20-55 years. Venkatesh et al.[17] reported a mean age of 41.8 years (range: 23-63), which demonstrated a relatively higher age-range compared to our study.

Previously, Rouviere et al.[12] reported a mean age of 26.7 years (range: 19-39 years) for healthy volunteers, Hines et al. (2010) observed a mean age of 28.1 years with age range of 22-40 years, Mannelli et al.[4] reported a mean age of 35±9 years (range: 29-58 years), Lee et al.[6] observed a mean age of 30.6±9.62 years, Rusak et al.[13] reported a mean age of 39.1 years (range: 24-45 years) and Obrzut et al.[11] reported a mean age of 21.6 years with a range of 20-28 years. Comparing to these studies, our study showed a relatively higher age range which may have been caused due to differences in demography.

The current study comprised 41 female subjects (68.3%) and 19 male subjects (31.7%). Male to female ratio was 1:2.2. Venkatesh et al.[17] reported 23 female volunteers and 18 male vounteers. The study performed by Obrzut et al.[11] reported 66 female (64.7%) and 36 male (35.3%) healthy volunteers. In these studies, as well, there were predominance of female subjects which is similar to our study.

In addition, Hines et al.[4] reported 7 female and 13 male healthy volunteers, Lee et al.[6] reported 16 female and 23 male healthy living liver donors, Mannelli et al.[8] reported 2 female and 9 male volunteers and Rouviere et al.[12] reported 4 female and 8 male volunteers which is not similar to our study.

The present study observed that mean BMI of the subjects was 21.9±1.25 Kg/m^2, ranging from 18.8 to 24.1 Kg/m^2. Venkatesh et al. [17] reported a mean BMI of 23.4 Kg/m^2 (range: 18.9 to 30 Kg/m^2), Hines et al.[4] observed a mean BMI of 22.9 Kg/m^2 with a range of 17.8 to 30.3 Kg/m^2. Mean BMI of our study is nearer to that of the studies mentioned.

In our study, the mean stiffness of the liver in the adult subjects ranged from 1.72 to 2.92 kPa with a mean±SD of 2.42±0.20 kPa. Previously, Venkatesh et al.[17] reported a mean stiffness of 2.09±0.22 kPa for healthy Asian volunteers (range: 1.68-2.42 kPa) which is nearly comparable to our study.

Rouviere et al.[12] reported a mean stiffness of 2.0±0.3 kPa for healthy volunteers which may be slightly lowered compared with the present study.

Mannelli et al.[8] reported a mean stiffness of 2.3±0.38 kPa for volunteers with no history of gastrointestinal, hepatobiliary or cardiovascular diseases with a range of 1.7-2.8 kPa which is almost similar to our study.

Lee et al.[6] observed liver stiffness values ranging from 1.54 to 2.87 kPa for Korean living liver donors which is comparable to the present study. The mean stiffness in the mentioned study was 2.05 kPa using 2-cm per slice method, 2.01 kPa with 1 cm-S method, 2.12 kPa using the 70% S method which is nearly similar to our study.

Rusak et al.[13] reported a mean stiffness of 2.30 kPa for healthy adults with a range of 1.56-2.75 kPa which is comparable to the present study.

Obrzut et al.[11] observed a mean stiffness of 2.14±0.28 kPa (range: 1.37-2.66 kPa) for healthy European volunteers. The result is nearly correspondent to our study.

Hines et al.[4] reported a mean stiffness of 2.44±0.06 kPa for healthy American volunteers which corroborate our study.

In the present study, it was observed that mean stiffness values for male subjects was 2.46±0.19 kPa with a range of 2.15 – 2.92 kPa, and for female subjects 2.40±0.21 kPa with a range of 1.72-2.66 kPa. Previously, Venkatesh et al.[17] reported a mean stiffness of 2.13±0.19 kPa (range: 2.03-2.22 kPa) and 2.07±0.18 kPa (range: 1.99-2.14 kPa) for male and female volunteers respectively, which stands nearer to our study. Obrzut et al.[11] reported a mean stiffness of 2.14±0.25 kPa (range: 1.54-2.54 kPa) and 2.14±0.30 kPa (range: 1.37-2.66 kPa) for male and female volunteers respectively, which remains closer to present study.

Our study did not find a statistically significant correlation between mean liver stiffness and age of the subjects (r=0.061, p=0.645). In a previous study, Venkatesh et al.[17] also did not observe any correlation between mean liver stiffness and age of the volunteers (r=0.042, p=0.8), which is similar to our study. Additionally, Obrzut et al.[11] reported no significant correlation of liver stiffness with age (r=-0.03, p=0.76) which is also consistent with the present study.

In this study, it was seen that there were no significant differences in mean liver stiffness between different age groups (p=0.305). Venkatesh et al.[17] also reported no significant differences in liver stiffness between different age groups (p=0.33), which is similar to current study.

Our study further analyzed the correlation between mean liver stiffness with sex (male-female) and observed that the difference was not statistically significant (p=0.272). In previous studies, Venkatesh et al.[17] and Obrzut et al.[11] reported no significant correlation between mean liver stiffness and sex with p values being 0.18 and 0.22 in their study results respectively, which is similar to our study.

Further analyses on our study presented that there was no correlation between mean liver stiffness and BMI (r=-0.036, p=0.782). Venkatesh et al.[17] also reported no significant correlation between mean liver stiffness and BMI (r=0.23, p=0.15), which is same as our result. In another study, Obrzut et al.[11] reported that mean liver stiffness was not influenced by BMI (r=0.001, p= 0.99) which concurs with the present study.

Conclusion

The purpose of this study was to determine normal liver stiffness values in adult Bangladeshi subjects by magnetic resonance elastography. The result manifested that the mean stiffness value for adult subjects was 2.42±0.20 kPa, with a range of 1.72-2.92 kPa. The results of this study implied that there was no discernible difference in mean liver stiffness by age, sex, or BMI. We believe that our study will contribute to the establishment of a reference value for normal liver stiffness with MR elastography for Bangladeshi population which will translate into a wider application of MRE in clinical practice and be useful for comparison of liver stiffness values in patients with liver diseases.

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