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# Role of Ultrasound Elastography in Determining Fibrosis In Patients With Chronic Liver Disease

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***Abstract:*** *Liver disease burden in India is enormous with 22.2 deaths/100,000 population attributed to cirrhosis. As a result of greater alcohol consumption, increased incidence of diabetes, obesity, hepatitis B and C infections, the incidence of chronic liver disease is increasing worldwide. Early detection of liver fibrosis is useful in early diagnosis and management of cirrhosis and its related complications. Since histopathology is an invasive tool, non-invasive technique like ultrasound elastography plays a vital role in estimating liver stiffness / fibrosis. The objective of this study was to evaluate the role of ultrasound elastography in assessment of fibrosis in patients with CLD. In this study, 50 cases of CLD and 50 healthy volunteers were subjected to ultrasound using B mode and then using shear wave based elastography. The findings between the cases and controls were compared and analysed statistically. Liver stiffness was found to be significantly higher in males (5.2 kPa) as compared to 4.8 kPa in females. Mean value of liver stiffness in chronic alcoholics was significantly higher than in non-alcoholics. Mean liver stiffness in cases of CLD was 10.83 kPa which was significantly higher than 5.05 kPa in healthy controls. Chronic hepatitis C was associated with higher liver stiffness (11.4 kPa) as compared to chronic Hepatitis B patients (9.7kPa). Majority patients of CLD (52%) had liver stiffness from 7-9.5 kPa corresponding to F2 fibrosis according to METAVIR grading. It was concluded that elastography provides an easy & non-invasive method for assessing and estimating liver stiffness in patients with CLD.*

***Keywords:*** *CLD - chronic liver disease, Fibroscan, Elastography, Chronic hepatitis B, Chronic hepatitis C, Liver stiffness*

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## I. INTRODUCTION

Liver disease burden in India is enormous with 22.2 deaths/100,000 population attributed to cirrhosis by the Global Health Observatory data from the World Health Organization. Chronic liver disease has various etiologies like viral infection of hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus, alcohol consumption, hepatotoxic drug ingestion, non-alcoholic fatty liver, autoimmune diseases, and cryptogenic hepatopathy being commonly encountered in daily practice.[1] Portal hypertension is a universal consequence of chronic liver disease that is responsible for most complications such as variceal bleeding, ascites, spontaneous bacterial peritonitis, hepatorenal and hepatopulmonary syndromes. Histologically, liver fibrosis develops and gradually progresses as a result of following a wound-healing response in patients with CLD. In particular, activation of cellular elements including myofibroblasts and stellate cells results in collagen deposition and subsequent development of CLD. [2] Diagnosis of chronic liver disease can be done via clinical, biochemical, pathological and radiological methods.

Numerous laboratory tests, and scores have also been proposed for non-invasive prediction of hepatic fibrosis in chronic HCV-infected patients like aspartate aminotransferase (AST) to platelet ratio (APRI), and fibrosis 4 index (FIB4). For people with chronic liver diseases, assessment of liver fibrosis is important for several reasons. Firstly, the degree of fibrosis is an indication of the severity of the underlying liver disease. Secondly, it may have prognostic significance. Pathologically, the gold standard for measuring liver stiffness is by liver biopsy, however it is an invasive procedure and associated with various risks and complications.

Radiological investigations like ultrasound elastography of the liver provides a useful method for assessment of stiffness of liver. Introduced in 1991, elastography is a non-invasive technique for evaluating the elastic properties of soft tissue either quantitatively or qualitatively. These include transient elastography, shear wave elastography, ARFI based elastography and real time tissue elastography. The normal value of Fibroscan ranges from 4.8 to 6.9 kilopascals(kPa). Transient elastography is highly reproducible with minimal inter-

observervariation. This study was conducted to determine the role of ultrasound elastography (transient elastography) in assessment of fibrosis in patients with CLD.

## II. Material And Methods

This prospective case control study was conducted in the Department of Radio-diagnosis, Guru Nanak Dev Hospital/Govt. Medical College, Amritsar, Punjab from June 2018 to November 2020 in which fifty patients with Chronic Liver Disease and fifty healthy volunteers (controls) were included in the study. Patients who were pregnant or breastfeeding patients with ascites, implantable cardiac devices, Patients patients with active extrahepatic infectious or inflammatory disorders or malignancy and patients with body mass index (BMI) greater than 40 $kg/m^2$ were excluded from the study.

Imaging Technique: Fifty healthy volunteers and fifty patients with chronic liver disease (chronic hepatitis B, C and chronic alcoholic hepatitis) were included, their relevant clinical details and biochemical investigations were recorded. They were subjected to greyscale ultrasound and liver elastography using Samsung RS80A Ultrasound system with CA1-7A probe. Liver stiffness (LS) was measured with the patient lying in the left lateral decubitus position and with right arm in abduction. Measurements were obtained from the right lobe of liver using the intercostal approach by placing the measuring box in right lobe of liver 1-2 cm below the liver capsule avoiding vessels. In each patient 10 valid LS measurements were obtained and the median of these values was calculated, the result was expressed in kilopascals KPa. The recorded data was analysed statistically.

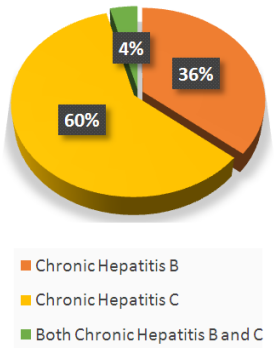
## III. Results

**Table 1 -** DEMOGRAPHIC PARAMETERS

| Age (Years) | Cases (Chronic hepatitis B and C) | Controls |
|---|---|---|
| **<20** | 1 (2%) | 0 (0%) |
| **21-30** | 4 (8%) | 6 (12%) |
| **31-40** | 16 (32%) | 17 (34%) |
| **41-50** | 9 (18%) | 14 (28%) |
| **51-60** | 10 (20%) | 12 (24%) |
| **>60** | 10 (20%) | 1 (2%) |
| **MeanAge (Years)** | 46.26 ± 13.79 | 42.54 ± 9.601 |
| **Sex** | | |
| **Males** | 36 (72%) | 25 (50%) |
| **Females** | 14 (28%) | 25 (50%) |
| **Chronic alcoholism** | 28 (56%) | 10 (20%) |

Table 1 shows that majority of controls (34%) and cases (32%) belonged to age group 31-40 years with mean age for cases being 46.26 years.In our study, 72% cases of chronic liver disease were males and 28% were females.56% of cases of chronic liver disease had history of chronic alcoholism whereas only 20% of healthy volunteers had history of alcoholism.

GRAPH 1 SHOWING DISTRIBUTION OF CHRONIC HEPATITIS B AND C IN CASES




Out of 50 chronic liver disease cases, 60% had chronic hepatitis C, 36% had chronic hepatitis B and 4% cases had both chronic hepatitis B & C.

**Table 2 -** DISTRIBUTION OF BIOCHEMICAL PARAMETERS IN CASES

| BIOCHEMICAL PARAMETERS | | No. of cases (%age) | p value |
|---|---|---|---|
| **Serum Bilirubin** | Increased | 10 (20%) | 0.001 |
| **ALT/AST** | Increased | 10 (20%) | 0.001 |
| **Platelet count** | Decreased | 12 (24%) | 0.000 |

Serum bilirubin was increased in 20% cases of CLD. Similarly deranged ALT and AST were seen in 20% cases. Platelet count was decreased in 24% cases.

**Table 3-** ULTRASOUND FINDINGS ON B MODE

| ULTRASOUND FINDINGS ON B MODE | | Cases | Control | p value |
|---|---|---|---|---|
| **Liver Size** | Normal | 25 (50%) | 50 | 0.52 |
| | Increased | 10 (20%) | 00 | |
| | Decreased | 15 (30%) | 00 | |
| **Outline** | Regular | 40 (80%) | 50 | 0.001 |
| | Irregular | 10 (20%) | 00 | |
| **Echotexture** | Normal | 14 (28%) | 50 | 0.002 |
| | Coarsened | 36 (72%) | 00 | |
| **Mean PV diameter (mm)** | | 11.91 ± 0.9 | 12.02 ± 0.6 | 0.487 |

Table 3 shows that 20% patients of chronic liver disease had hepatomegaly and 30% cases had decreased/shrunken liver size. Rest of the patients had normal liver size on B mode ultrasonography. All the normal healthy controls had a normal liver size.20% cases of chronic liver disease had irregular outline of liver and 80% cases had normal liver outline. All the healthy volunteers had normal liver outline. 72% cases of chronic liver disease had a coarsened echotexture on B mode ultrasonography whereas 28% cases had a normal liver echotexture. All the healthy volunteers had normal liver echotexture. Mean PV diameter was 11.9mm for cases and 12.02mm for controls.

**Table 4-** LIVER STIFFNESS MEASURED BY FIBROSCAN (IN KILOPASCALS) IN CASES AND CONTROLS

| Liver Stiffness (kPa) | Cases | Controls | p value |
|---|---|---|---|
| **2.5-≤7** | 5 (10%) | 50 (100%) | |
| **7-≤9.5** | 26 (52%) | 0 (0%) | |
| **9.5-≤12.5** | 5 (10%) | 0 (0%) | |
| **>12.5** | 14 (28%) | 0 (0%) | |
| **Mean ± S.D** | 10.83 ± 0.4 | 5.05 ± 0.6 | 0.001 |

Table 4 depicts that mean value of liver stiffness in cases of chronic liver disease was 10.83 kPa ± 0.4 SD. Mean value of liver stiffness in control group was 5.05 kPa ± 0.6 SD. There was statistically significant difference in the liver stiffness between cases and control groups with p value 0.001. In the cases group, the values of liver stiffness ranged from 4.1kPa to 25.6kPa. In the control group, the values of liver stiffness ranged from 3.8kPa to 6.7kPa.

**Table 5-** CORRELATION OF CHRONIC ALCOHOLISM WITH LIVER STIFFNESS MEASUREMENTS

| Chronic alcoholism | Number of cases | Mean LS (kPa) | Std. Deviation | p value |
|---|---|---|---|---|
| **Yes** | 38 (38%) | 10.1737 | 5.55993 | 0.001 |
| **No** | 62 (62%) | 6.5774 | 2.99920 | |

Table 5 shows that out of total 100 people included in the study, (50 cases and 50 controls), 38% had history of chronic alcoholism and 62% did not have history of chronic alcoholism. Mean liver stiffness in cases with chronic alcoholism was 10.17 kPa. Mean liver stiffness in cases without any history of chronic alcoholism was 6.5 kPa. This data was statistically significant with p value less than 0.05.

**Table 6-** COMPARISION OF LIVER STIFFNESS AMONG CASES OF CHRONIC HEPATITIS B, C AND CHRONIC ALCOHOLICS

| Cases | Number of cases | Mean LS | p value |
|---|---|---|---|
| **Chronic hepatitis B** | 20 | 9.77 | 0.04 |
| **Chronic Hepatitis C** | 32 | 11.4 | 0.001 |
| **Chronic alcoholics** | 38 | 10.1 | 0.001 |

Table 6 shows that there was significant difference in liver stiffness measurements in patients of chronic hepatitis B, chronic hepatitis C and chronic alcoholic patients. P value calculated was less than 0.05 which was statistically significant.

**Table 7-** COMPARISION OF LIVER STIFFNESS BETWEEN MALES AND FEMALES

| CONTROLS | Number of subjects | Mean LS (kPa) | Standard Deviation | p value |
|---|---|---|---|---|
| **Male** | 25 | 5.29 | 0.63 | 0.011 |
| **Female** | 25 | 4.80 | 0.66 | |
| **CASES** | | | | |
| **Males** | 36 | 11.07 | 5.41 | 0.46 |
| **Females** | 14 | 10.22 | 2.80 | |

Table 7 shows that mean value of liver stiffness in healthy males was 5.2 kPa as compared to 4.8 kPa in healthy females. In cases of CLD, mean value of liverstiffness among males was 11.07 kPa as compared to 10.22 kPa in females.

**Table 8-** DISTRIBUTION OF LIVER STIFFNESS IN CHRONIC LIVER DISEASE CASES CORRESPONDING TO THEIR HISTOPATHOLOGICAL GRADING (METAVIR GRADING)

| LS (kPa) | METAVIR grading | Hep B | Hep C | Both hep B & C | Total |
|---|---|---|---|---|---|
| **2.5-≤7** | F0/F1 | 1 (2%) | 4 (8%) | - | 5 (10%) |
| **7-≤9.5** | F2 | 12(24% | 13(26%) | 1 (2%) | 26 (52%) |
| **9.5-≤12.5** | F3 | 1 (2%) | 3 (6%) | 1 (2%) | 5 (10%) |
| **>12.5** | F4 | 4 (8%) | 10 (20%) | - | 14 (28%) |

Table 8 shows that out of the 50 cases of chronic liver disease, majority patients (52%) had liver stiffness from 7-9.5 kPa corresponding to F2 fibrosis (METAVIR grading). 28% cases had liver stiffness more than 12.5 kPa corresponding to F4 fibrosis according to METAVIR grading. The data was statistically significant with p value less than 0.05.

## IV. Discussion

In our study most of the cases (32%) and controls (34%) belonged to the age group 31-40 years. Mean age for the cases was 46.46 years. Similarly, in a study conducted by Sporea I et al[3], mean age among patients of chronic Hepatitis C was 49.7 ± 10.2 years.Mean age for the healthy controls was 42.54 years. In a study conducted by Fung J et al on 530 healthy volunteers, mean age of the healthy controls was 37 years[4]. 72% cases were males as compared to 28% females with chronic liver disease. Similarly, in a study done by Foucher J et al[5], males were predominant (67%). This could be attributed to males being more at risk for having chronic hepatitis B and C due to increased intravenous drug abuse and alcohol intake as compared to females. In our study, majority of the cases (92%) and controls (88%) had BMI 22-25 Kg/sq.meters. Mean BMI was similar for the cases and control group, i.e., 22.63 kg/m$^2$.In a similar study conducted by Fung J et al[4], mean BMI of cases was 20.6 kg/m$^2$

In our study, in patients of chronic liver disease, 56% cases had history of chronic alcoholism. In a study conducted by Sawaf B et al, 42% cases of chronic liver disease had history of chronic alcoholism. Higher percentage of chronic alcoholism may be due to the high alcohol consumption in state of Punjab[6].

In our study, out of total cases of chronic liver disease, 60% patients had chronic hepatitis C and 36% patients had chronic hepatitis B. In a similar study conducted by Sporea I et al, percentage of Hepatitis C cases (69%) was significantly more than Hepatitis B cases[3]. This is in accordance with the results of our study. In another study conducted by Grewal U et al[7], prevalence of chronic hepatitis C was 65%.

Biochemical parameters including serum bilirubin, ALT, AST were deranged in only 20% cases of chronic liver disease. This can be attributed to the fact that ALT, AST markers keep fluctuating in the course of the chronic liver disease and generally become normal in values in cases of long-standing chronic hepatitis, which was seen in our study. B mode ultrasonography was conducted for assessment of liver parameters in cases of chronic liver disease. 20% patients of chronic liver disease had hepatomegaly and 30% cases had decreased/shrunken liver size. Rest of the patients had normal liver size on B mode ultrasonography. Our results signify that in CLD, one may have an enlarged to a fibrosed liver depending upon severity and chronicity of underlying disorder. These findings are similar to the study done by Hanif *etal*[8].

20% cases of chronic liver disease had irregular liver outline. A study done by Mahjabeen*et al*[9] showed 32% cases of CLD with irregular liver outline. In our study, 72% cases of chronic liver disease had coarsened echotexture on B mode ultrasonography. Similarly, coarsening of hepatic parenchymal echotexture was seen in 85% cases of CLD in a study by MaajiS et al[10]. Since liver echotexture has a greater subjectivity in terms of observation, the findings may differ in different studies.

Elastography was conducted among healthy controls and their liver stiffness was calculated. In the control group comprising of healthy volunteers, the values of liver stiffness ranged from 3.8kPa to 6.7kPa. Mean value of liver stiffness in control group was 5.05 kPa +/- 0.6 SD. Similar results were seen in a study conducted by Alsebaey et al among healthy people, in which the mean LS was 4.3 ± 1.2 kPa[11]. Another study conducted by Fung J et al showed that mean LS in healthy population was 4.1 kPa. In our study, mean value of liver stiffness in healthy males was 5.2 kPa and among healthy females was 4.8 kPa. The study conducted by Fung J et al also showed similar results in which the liver stiffness was higher in males (4.3 kPa) compared with females (4.0 kPa)[4].

It was found that mean value of liver stiffness in chronic alcoholics was 10.17 kPa which was significantly higher than those who were not alcoholic (6.5kPa). This indicates that chronic alcohol intake is an important risk factor for increased liver stiffness and in pathogenesis of CLD.

We found that mean value of liver stiffness in all cases of CLD was 10.83 kPa +/- 0.4 SD with values ranging from 4.1kPa to 25.6kPa. In a similar study by Sporea I et al[3], the mean value of LS in the subgroup of 191 patients with valid measurements was 8.45 ± 4.96 kPa, ranging from 2.3 to 38 kPa. A study conducted by Sun J et al[12] showed mean liver stiffness of 10.6 kPa among patients with CLD indicating fibrosis greater than F2 METAVIR grade.

Patients with chronic Hepatitis C had mean liver stiffness 11.4 kPa as compared to 9.7 kPa in patients with chronic Hepatitis B with a statistical significant p value. Similar results were seen in study by Sporea I et al in which chronic Hepatitis C patients had higher mean liver stiffness (8.9 kPa) as compared to 8.1 kPa in chronic Hepatitis B patients[3]. The findings indicate that chronic Hepatitis C is more strongly associated with increased liver stiffness in patients of CLD.

The findings of elastography (liver stiffness) were tabulated according to the METAVIR grading which correlates histopathological changes of fibrosis with liver stiffness. Majority patients (52%) had liver stiffness from 7-9.5 kPa corresponding to F2 fibrosis. 28% cases had liver stiffness more than 12.5 kPa corresponding to F4 fibrosis. Similar observations were made by Sporea I et al[3] where majority of patients with Hepatitis B and Hepatitis C had liver stiffness corresponding to F2 fibrosis.

## V. Conclusion

Since elastography provides an easy & non-invasive method for assessing and estimating liver stiffness in patients with CLD, it can help in early detection of complications and can prevent unnecessary interventions like biopsy which are invasive. Hence, ultrasound elastography provides a safe and sensitive method for assessment of fibrosis in patients with chronic liver disease.

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