ROLE OF FIBROSCAN IN ASSESSING THE EXTENT OF LIVER INVOLVEMENT AMONG CHRONIC HEPATITIS B AND C CASES

Pendyala Jyothish, Dasara Vanisree, Durbha Satyanarayana Murty, Kolli Prasanthi

Chronic liver diseases (CLD) cause significant morbidity and mortality worldwide, accounting for approximately 2 million deaths annually. The majority of CLDs include alcoholic liver disease, chronic viral hepatitis, including hepatitis B and C, non-alcoholic fatty liver disease (NAFLD), and hemochromatosis. Of these, hepatitis B virus (HBV) and hepatitis C virus (HCV) infections account for a substantial proportion of liver diseases which is responsible for liver damage ranging from minor disorders to liver cirrhosis and hepatocellular carcinoma (HCC). Fibroscan is a novel non-invasive method for assessing hepatic fibrosis by measuring liver stiffness.

The aim. The present study was conducted to know the prevalence of blood-born viral pathogens (HBV, HCV) among patients with chronic liver diseases (CLD) and also to assess the role of Fibroscan and liver function tests (LFT) in evaluating the extent of chronic liver disease.

Material and methods: The present study comprised 100 chronic liver disease patients attending the gastroenterology department. All the chronic liver disease cases were tested for Hepatitis B and Hepatitis C viral infections using a rapid Immunochromatography assay. Simultaneously they were subjected to liver function tests and fibroscan to assess the extent of fibrosis by staging from F0 to F4.

Results: When screened for bloodborne viral pathogens, 46 % were HBV positive, 10 % were HCV, and none were HIV positive. No co-infection was detected. HBV was identified as the most typical cause of CLD in about 46 %, followed by non-viral/non-infectious (alcoholic, metabolic, autoimmune) cause in 44 % and 10 %, the cause for CLD was HCV. As per fibroscan results, 80 % of HCV and 39 % of HBV patients were in the stage of cirrhosis/advanced fibrosis.

Conclusion: HBV was the predominant cause of CLD. Liver stiffness has recently been shown to be a good predictor of clinical outcomes. A fibroscan will help in the decision-making process in staging the disease and choice of treatment in viral hepatitis cases

Keywords: chronic liver diseases (CLD), hepatitis B viral infections, bloodborne, advanced fibrosis, Fibroscan, liver function tests (LFT), transient elastography


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1. Introduction
Chronic liver diseases (CLD) cause significant morbidity and mortality worldwide. Multiple etiological factors lead to a similar clinicopathological syndrome in CLDs, although the progression and clinical course rates may differ [1]. The liver disease accounts for approximately 2 million deaths per year worldwide, one million due to complications of cirrhosis and one million due to viral hepatitis and hepatocellular carcinoma. Cirrhosis is currently the 11th most common cause of death globally, and liver cancer is the 16th leading cause of death; combined, they account for 3.5 % of all deaths worldwide. In addition, cirrhosis is within the top 20 causes of disability-adjusted life years and years lost, accounting for 1.6 % and 2.1 % of the worldwide burden [2].

Most chronic liver diseases in the developing world include alcoholic liver disease, chronic viral hepatitis, including hepatitis B and C, non-alcoholic fatty liver disease (NAFLD), and hemochromatosis [3]. Hepatitis B virus (HBV) and hepatitis C virus (HCV) account for 96 % of all deaths related to viral hepatitis [4]. These viruses are responsible for liver damage ranging from minor disorders to liver cirrhosis and hepatocellular carcinoma (HCC) [5]. Assessment of liver fibrosis has been a cornerstone of evaluating patients with any chronic liver disease (CLD) for therapeutic decision-making, prognostication and evaluation of treatment response [6]. WHO's global target for viral hepatitis for 2030 is to reduce the incidence of new chronic infections by 90 % and reduce attributable mortality by 65 % from the 2015 baseline.

Transient elastography (TE, Fibroscan) is a novel non-invasive method that has been proposed to assess hepatic fibrosis in patients with chronic liver disease by measuring liver stiffness. TE is a rapid and user-friendly technique that can be easily performed at the bedside or in the outpatient clinic with immediate results and good reproducibility [7].

The aim. The present study was conducted to know the prevalence of blood-born viral pathogens (HBV, HCV) among patients with chronic liver diseases (CLD) and also to assess the role of fibroscan and liver function tests (LFT) in evaluating the extent of chronic liver disease.
2. Material and methods

This was a prospective hospital-based cross-sectional study carried out over a period of one year from 2018–19 in the department of Microbiology & Department of Gastroenterology, Guntur Medical College/Hospital, Guntur. Institution ethics committee approval was obtained (GMC/IEC/079/2017).

100 clinically diagnosed chronic liver disease patients visiting the Gastroenterology unit of Government general hospital under Guntur medical college were enrolled in the study. Patients who were not willing to participate in the study were excluded. After obtaining consent from each patient, relevant sociodemographic and possible risk factors data was collected from all clinically diagnosed patients with chronic liver disease using a predesigned questionnaire. Under strict aseptic conditions, 5 ml of blood sample was collected from each patient, serum separated and stored at −20 °C. All the serum samples were screened for HBsAg and anti HCV antibodies using rapid Immunochromatography assay using Alere Trueline rapid test kits manufactured by Alere Medical Pvt Ltd. All the serum samples were also screened for HIV antibodies using the Tridot test. Simultaneously liver function tests (LFT) test results for Alanine Aminotransaminase (ALT normal ranges 8-45U/L), Aspartate Aminotransferase (AST normal ranges 7-56 U/L), Alkaline phosphatase (ALP normal ranges 44-147 IU/L), serum Bilirubin (normal ranges 0.2–0.8 mg/dl) were obtained. All the patients were subjected to Fibroscan Transient elastography (EchoSens, Paris, France), which measures liver stiffness to assess the extent of fibrosis by staging from F0 to F4, which is a test that measures the amount of fibrosis (thickening or scarring of tissues) in the liver in kilo Pascal’s (or kPa) ranging from 2 to 75. The norm range for a scan is between 2–7 kPa. The typical average result is 5.3 kPa [8]. The scarring has 4 stages [8]:

- F0 – F1 – no/minimal scarring (<7)
- F2 – moderate fibrosis (7.1–9)
- F3 – severe fibrosis (9.1–14)
- F4 – cirrhosis/advanced fibrosis (>14)

Data were entered in Microsoft excel, and analysis was done using SPSS version 20. Descriptive statistical analysis was done. Results on continuous measurements are presented as Mean & Standard Deviation. Results on categorical measurements are presented as percentages.

3. Results

The study included 100 clinically diagnosed chronic liver disease (CLD) patients.

Out of 100 CLD patients, most of them were above 50 years (30 %), followed by 21–30 years (28 %) group. The mean age of patients in the study is 41.74 years (Table 1).

In this study, 70 % of patients were males, and 30 % were females (Table 2).

Among the 100 CLD patients, the predominant cause of CLD was HBV (46 %). In 10 %, it was HCV. 44 % were negative for both HBV and HCV. All of them were negative for HIV antibodies. The cause of CLD might be other than HBV and HCV, which could be alcoholic, metabolic, or autoimmune (Table 3).

### Table 1

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>No of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>0</td>
<td>0 %</td>
</tr>
<tr>
<td>11–20</td>
<td>4</td>
<td>4 %</td>
</tr>
<tr>
<td>21–30</td>
<td>28</td>
<td>28 %</td>
</tr>
<tr>
<td>31–40</td>
<td>16</td>
<td>16 %</td>
</tr>
<tr>
<td>41–50</td>
<td>22</td>
<td>22 %</td>
</tr>
<tr>
<td>51 &amp; above</td>
<td>30</td>
<td>30 %</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100 %</td>
</tr>
</tbody>
</table>

### Table 2

<table>
<thead>
<tr>
<th>Gender</th>
<th>No of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>70</td>
<td>70 %</td>
</tr>
<tr>
<td>Females</td>
<td>30</td>
<td>30 %</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100 %</td>
</tr>
</tbody>
</table>

### Table 3

<table>
<thead>
<tr>
<th>Cause of CLD</th>
<th>No of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV</td>
<td>46</td>
<td>46 %</td>
</tr>
<tr>
<td>HCV</td>
<td>10</td>
<td>10 %</td>
</tr>
<tr>
<td>Non-viral/non-infectious (alcoholic, metabolic, autoimmune)</td>
<td>44</td>
<td>44 %</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100 %</td>
</tr>
</tbody>
</table>

Among HBV positive patients, the predominant (57 %) were in the 21–30 years age group & 50 % in the 31–40 years age group. In HCV, 20 % were 51 years and older (Table 5).

### Table 4

<table>
<thead>
<tr>
<th>Virus</th>
<th>No of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV positive</td>
<td>46</td>
<td>46 %</td>
</tr>
<tr>
<td>HCV positive</td>
<td>10</td>
<td>10 %</td>
</tr>
<tr>
<td>HBV, HCV co-infection</td>
<td>0</td>
<td>0 %</td>
</tr>
</tbody>
</table>

### Table 5

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>No of cases</th>
<th>HBV</th>
<th>HCV</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>0 (0 %)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>11–20</td>
<td>4 (4 %)</td>
<td>2 (50 %)</td>
<td>0</td>
</tr>
<tr>
<td>21–30</td>
<td>28 (28 %)</td>
<td>16 (57 %)</td>
<td>0</td>
</tr>
<tr>
<td>31–40</td>
<td>16 (16 %)</td>
<td>8 (50 %)</td>
<td>0</td>
</tr>
<tr>
<td>41–50</td>
<td>22 (22 %)</td>
<td>8 (36 %)</td>
<td>4 (18 %)</td>
</tr>
<tr>
<td>51 &amp; above</td>
<td>30 (30 %)</td>
<td>12 (40 %)</td>
<td>6 (20 %)</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>46</td>
<td>10</td>
</tr>
</tbody>
</table>

Of the 46 HBV-positive CLD patients, 34 (73.9 %) were males, and 12 (26 %) were females. Out of 10 HCV positive patients, 8 (80 %) were males 2 (20 %) were females (Table 6).
Elevation of serum Aminotransferases (60 %) and Alkaline phosphatase (40 %) was observed in HCV-positive patients. All the HCV patients (100 %) had abnormal LFT. Among HBV, 30.4 % and 8.6 % had elevated serum aminotransferase and alkaline phosphatase levels. Only 39 % of HBV had abnormal LFT results (Table 7).

Table 6

<table>
<thead>
<tr>
<th>CLD cases</th>
<th>HBV</th>
<th>HCV</th>
<th>Non-viral</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males (70)</td>
<td>34 (73.9 %)</td>
<td>8 (80 %)</td>
<td>28 (63.6 %)</td>
<td>70</td>
</tr>
<tr>
<td>Females (30)</td>
<td>12 (26 %)</td>
<td>2 (20 %)</td>
<td>16 (36.3 %)</td>
<td>30</td>
</tr>
<tr>
<td>Total</td>
<td>46</td>
<td>10</td>
<td>44</td>
<td>100</td>
</tr>
</tbody>
</table>

Among HCV, results of Fibroscan showed 20 % in the stage of moderate to severe fibrosis and 80 % in the cirrhosis/advanced fibrosis stage. In HBV-positive patients, 13 % had moderate to severe fibrosis and 39 % in cirrhosis/advanced fibrosis stage (Table 8).

Table 7

<table>
<thead>
<tr>
<th>CBD</th>
<th>Liver function tests (LFT)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Amino transferases</td>
<td>Alkaline phosphatase</td>
</tr>
<tr>
<td>HBV(n=46)</td>
<td>14 (30.4 %)</td>
<td>4 (8.6 %)</td>
</tr>
<tr>
<td>HCV(n=10)</td>
<td>6 (60 %)</td>
<td>4 (40 %)</td>
</tr>
<tr>
<td>Non-infectious (n=44)</td>
<td>22 (50 %)</td>
<td>10 (22.7 %)</td>
</tr>
</tbody>
</table>

Table 8

<table>
<thead>
<tr>
<th>CBD</th>
<th>Fibroscan</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Moderate – severe fibrosis</td>
<td>Cirrhosis/advanced fibrosis</td>
</tr>
<tr>
<td>HBV(n=46)</td>
<td>6 (13 %)</td>
<td>18 (39 %)</td>
</tr>
<tr>
<td>HCV(n=10)</td>
<td>2 (20 %)</td>
<td>8 (80 %)</td>
</tr>
<tr>
<td>Non-infectious (n=44)</td>
<td>6 (13.6 %)</td>
<td>16 (36.4 %)</td>
</tr>
</tbody>
</table>

4. Discussion

Viral hepatitis is a cause of major health care burden in India and is now equated as a threat comparable to the "big three" communicable diseases – HIV/AIDS, malaria and tuberculosis. Hepatitis B virus (HBV) and Hepatitis C virus (HCV) are predominantly spread via the parenteral route and are notorious for causing chronic hepatitis, which can lead to grave complications, including cirrhosis of the liver and hepatocellular carcinoma (HCC). Around 400 million people all over the world have chronic hepatitis. In order to reduce the complications associated with chronic Hepatitis B (CHB) infection, it is imperative to suppress viral replication before developing cirrhosis and HCC [9]. Historically, viral hepatitis has been the leading aetiology for CLD. The absolute number of CLD cases (inclusive of any stage of disease severity) is estimated at 1.5 billion worldwide [10]. Progressive hepatic fibrosis with the development of cirrhosis is a feature of almost all chronic liver diseases. Approximately 10–20 % of patients with chronic hepatitis C virus infection have cirrhosis at first clinical presentation, and as many as 20–30 % of those who do not have cirrhosis will eventually develop this condition and its complications within one or more decades. Transient elastography or Fibroscan is a novel, rapid, and non-invasive technique which measures liver stiffness [11].

In the present study, most CLD patients were above 50 years (30 %), followed by the 21–30 years (28 %) group. The mean age of the study group was 41.74 yrs. 70 % were males, and 30 % were females. In the study by Vilas BN et al. (2018, India), 67 (83.75 %) were males, and 13 (16.25 %) were females. The maximum number of chronic liver disease patients were in the age group of 41–50 years (41.30 %), followed by 31 – 40 years (23.80 %) [12].

The highest prevalence of HBV (57 %) was seen in the age group of 21–30 years, followed by 50 % in the 31–40 age group. This study correlated with studies carried out by Abel Girma Ayele et al. (2013, Ethiopia), who reported the mean age as 40.99 years, with the prevalence of HBV highest (61 %) in the age group of 28–37 years [5] whereas Partha S. Mukherjee et al. (2017, Kolkata) reported Median age as 43 years [1].

In this study HBV positive in 73.9 % (n=46) and HCV in 80 % (n=10) of males and in females HBV and HCV positive in 26 % and 20 % respectively. The results are similar to those of Shannugam Saravanan et al. (2008, Chennai), who reported HBV positive in 72 % and HCV in 80 % of males. Females infected with HBV and HCV were only 28 % and 20 %, respectively [13].

In our study, HBV and HCV were prevalent among 46 % and 10 % of CLD patients. Partha S. Mukherjee et al. (Kolkata, 2017) reported a 40.5 % prevalence of HBV and 10.9 % of HCV [1], similar to our study. Abel Girma et al. (2013) from Ethiopia has a prevalence of 35.8 % HBV and 22.5 % HCV [5]. None of the CLD patients in our study had dual infections of both HBV and HCV. No dual hepatitis B and C virus co-infection was found in the study by Anirban Kündu et al. (2015 India) [14]. Abel Girma Ayele et al. (2013 Ethiopia) reported dual infection in 2.5 % of CLD patients [5]. The difference in the magnitude of co-infection among these studies and our study could be attributable to the
geographical variation, study population and difference in methodology.

Abnormal LFT, i.e., the elevation of serum Amino transferases (60 %) and Alkaline phosphatase (40 %), was observed in HCV-positive patients in this study. Patrick Marcellin et al. (2002) reported that high serum alanine aminotransferase (ALT) levels are associated with a higher risk of fibrosis progression, and worsening of fibrosis is uncommon in patients with persistently normal serum aminotransferase levels [15].

The results of the Fibroscan showed cirrhosis/advanced fibrosis in 80 % of HCV & 39 % of HBV. In HCV, any level of virus replication can be associated with liver injury. In contrast, in chronic HBV infection, a threshold exists, approximately 10^3 to 10^7 IU/ml, below which liver injury is negligible or absent (Mandell Douglas) [16]. Alcohol consumption, age at infection and male gender have been identified as risk factors for faster fibrosis progression in patients with HCV [17].

The American Association for the Study of Liver Diseases (AASLD) practice guidelines for managing hepatitis C virus (HCV) infection state that patients with stage 3 or more significant fibrosis are an essential group to treat because they have the most urgent need for treatment. Fibroscan can be used to stratify patients in terms of their need for treatment urgency because it can accurately detect patients with advanced fibrosis [18–20].

Limitations of the study: Fibroscan method is limited as screening tool in medical practice because of the invasive nature of the biopsies. Tests are limited in their ability to reflect the entirety of liver function in CHB patients fully.

TE has limitations and is challenged by other technologies to measure liver stiffness, such as ARFI and MR elastography, whose place in clinical practice remains to be defined.

Prospects for further research: Significant progress has been made over the past decade in the non-invasive assessment of liver disease in patients with hepatitis B or C, but there is no perfect method. On the one hand, there is increasing awareness that liver biopsy is an imperfect standard. On the other hand, an increasing number of non-invasive methods are available: TE, FibroTest, and APRI are the most widely used and validated worldwide.

It is vital to investigate the prognostic value of non-invasive methods of fibrosis detection, particularly TE, for patients with cirrhosis; these tests could be used to better classify patients with cirrhosis and assign them to different risk categories for clinical outcomes.

Other promising techniques, such as supersonic shear imaging or spleen stiffness measurements, could also become available and deserve further evaluation. In addition, it has been proposed that non-invasive methods be used to screen the general population for cirrhosis.

However, this approach is not likely to be cost-effective, given the low prevalence of cirrhosis in the general population.

5. Conclusion

46 % of patients tested for bloodborne viral infections had HBV, 10 % had HCV, and none had HIV. Co-infection was not found. 34 (73.9 %) of the 46 HBV-positive CLD patients were men, and 12 (26 %) were women. Eight (80 %) of the ten HCV-positive patients were men, and two (20 %) were women. According to fibroscan data, 39 % of HBV and 80 % of HCV patients had advanced fibrosis or cirrhosis. Liver stiffness has recently been shown to be a good predictor of clinical outcomes over time. Fibroscan will help in the decision-making process in staging the disease and choice of treatment which is also crucial for prognosis and surveillance.

Conflict of interest

The authors declare that they have no conflict of interest concerning this research, whether financial, personal, authorship or otherwise, that could affect the research and its results presented in this article.

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