Original Article

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VALIDITY OF ULTRASOUND IN DIAGNOSIS OF LIVER FIBROSIS RESULTING FROM CHRONIC VIRAL HEPATITIS

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ABSTRACT

Objective: To determine the validity of ultrasound in diagnosis of liver fibrosis associated with chronic viral hepatitis, considering histopathological findings as gold standard.

Study Design: Validation study.

Place and Duration of Study: Department of Radiology, Military hospital Rawalpindi, from March 2007 to February 2008.

Patients and Methods: Patients with positive laboratory findings of viral hepatitis were sonographically evaluated in Radiology department in lying position with 2–5 MHz frequency convex and 5–12 MHz frequency linear probes of Aloka prosound (ssd) 5500 ultrasound machine. An Ultrasound scoring system using both the low and high frequency probes was performed by evaluating the edge, surface and parenchymal texture of the liver. Each score was obtained by evaluating three parameters; the bluntness of the liver edge, the irregularity of the surface and coarseness of the parenchymal texture were evaluated and then compared with the histological findings.

Results: Amongst 50 patients with history of chronic viral hepatitis, 31(62%) were males and 19 (38%) were females. Ages of patients ranged between 26-60 years (mean 40.8 years). The US (ultrasound) accumulated scores of the liver edge, liver surface and liver parenchymal texture were compared with the fibrosis stage obtained based on the biopsy findings. The accumulated US scores of these three parameters (fibrosis stage 0-IV- No fibrosis, mild, moderate and sever fibrosis) however, were found to be the most reliable indicator. Thirty Two (64%) patients showed true positive, 4 patients (08%) showed false positive, 09 (18%) patients showed true negative and 05 patients (10%) patients showed false negative results. (Table .1)

Sensitivity, Specificity, positive predictive values, Negative predictive values and accuracy of Ultrasound in diagnosis of liver fibrosis were calculated to be 86.48%, 69.23%, 88.88 %, 64.28% and 82% respectively. (Table.2)

Conclusion: Ultrasound evaluation of the liver fibrosis stage based on the scoring system using both low and high frequency probes has been found to be a reliable and effective alternative to the histological staging in chronic liver disease.

Key words: Chronic viral hepatitis, Fibrosis, Ultrasound, Validity.

INTRODUCTION

Chronic hepatitis virus B or C infection results in damage to hepatocytes and may eventually lead to liver fibrosis, cirrhosis or hepatocellular carcinoma[1,2]. The diagnosis of liver fibrosis and cirrhosis in patients with chronic viral hepatitis is of therapeutic and prognostic importance.[3] A liver biopsy is considered to be the gold standard for diagnosing liver fibrosis stage and predicting the outcome of diseases. Although a percutaneous liver biopsy is relatively safe, it is still associated with a risk of complications, patient discomfort and a high cost.[4] In addition, liver biopsy examinations may lead to false negative results due to inadequate liver tissue sampling. Therefore, there is a need to develop a simple, reliable and non-invasive modality in order to assess the liver fibrosis stage.[5]

Ultrasound (US) is a non-invasive, inexpensive and easily repeatable modality and has been used as the most important and valuable diagnostic tool for detecting hepatocellular carcinoma during the follow-up of patients with viral hepatitis.[6]

An ultrasound evaluation of the liver fibrosis stage of chronic liver disease has been

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performed by assessing various ultrasound factors such as the liver size, the bluntness of the liver edge, the coarseness of the liver parenchyma, nodularity of the liver surface.[7]

However, the conventional definition of the fibrosis stage of the liver based on evaluation of these ultrasound factors is imperfect and lacks accuracy and reliability. These findings also depend largely on the equipment used. [8]

Recent advances in ultrasound technology have improved the diagnostic accuracy for fibrosis in patients with chronic liver disease.[9] Therefore, it is beneficial to conduct a study for accuracy of Ultrasound in diagnosing various stages of liver fibrosis in patients with chronic viral hepatitis and compare the results obtained from this study with the histopathological findings. The aim of this study was to adopt a standard procedure of performing ultrasound as a preliminary diagnostic tool for staging liver fibrosis in patients of chronic viral hepatitis and follow up of those patients diagnosed for liver fibrosis.

PATIENTS AND METHODS

This validation study was conducted in Radiology department Military hospital Rawalpindi from March 2007 to February 2008.

Patients were selected with the following inclusion and exclusion criteria:

Inclusion Criteria:

- Patients of all ages and both genders.
- History of chronic liver disease, based on the detection of persistently high levels of aminotransferase.
- Absence of clinical and/or biochemical signs of decompensated liver diseases (jaundice, ascites or encephalopathy)
- No previous histopathological diagnosis.
- Consenting and cooperative patients giving informed consent.

Exclusion Criteria:

- Unwilling and non-cooperative patients.
- Patients who have already undergone liver biopsy

The ultrasound findings from right and left lobes of liver were recorded as under:-

The ultrasound score was determined from the right and left lobes and the average score for each parameter was calculated as follows:

1. Liver edge:

- Score 0 for sharp
- Score 1 for mildly blunted
- Score 2 for blunted

2. Liver surface:

- Score 0 for smooth
- Score 1 for mildly irregular
- Score 2 for irregular
- Score 3 for highly irregular

3. Liver parenchymal texture:

- Score 0 for fine
- Score 1 for mildly coarse
- Score 2 for Coarse
- Score 3 for highly coarse

Patients with an accumulated score of 6 or more were placed in category of severe fibrosis {stage-IV (Figure.1)}

Patients with score 3 to 5 with moderate fibrosis.

Patients with score less than 3 were categorized to have mild fibrosis.

Score 0 showed no sonographic evidence of fibrosis.

On the basis of these findings liver fibrosis was labeled as normal/ no fibrosis, mild, moderate and severe. Liver biopsy was performed with in 15 days after the ultrasound examination in all suspected cases of chronic liver disease. Ultrasound based diagnosis of chronic viral hepatitis was compared with histopathological findings.

RESULTS

In this study 50 patients with positive laboratory findings of chronic viral hepatitis were examined sonographically in the Radiology department in lying position with 2–5 MHz frequency convex and 5–12 MHz

frequency linear probes. Out of 50 patients 31(62%) were males and 19 (38%) were females (Figure.2). Age range was between 26-30years with mean 40.8 years. (Figure.3) Thirty Two (64%) patients showed true positive, Four patients (08%) showed False Positive, 09 (18%) patients showed true negative and 05 patients (10%) patients showed false negative results. (Table 1)

Table.1: Different Stages of Histopathology Based Liver Fibrosis

Different Stages of Ultrasound based Liver Fibrosis	No Fibrosis	Mild Fibrosis	Moderate Fibrosis	Severe Fibrosis
No Fibrosis	09	02	0	0
Mild Fibrosis	01	13	02	0
Moderate Fibrosis	0	02	12	01
Severe Fibrosis	0	0	01	07

Table.2: 2x2 Table for calculating sensitivity, specificity, positive predictive value, negative predictive values and accuracy of Ultrasound in diagnosis of liver fibrosis

	Histopathology	
Ultrasound	**Positive**	**Negative**
Positive	(TP) a 32	(FP)b 04
Negative	(FN) c 05	(TN) d 09

TP = True Positive
FP = False Positive
FN = False Negative

Diagnostic measures were calculated through table-2, sensitivity, specificity, positive predictive value, negative predictive value and accuracy of ultrasound in diagnosis of liver fibrosis were 86.48%, 69.23%, 88.88 %, 64.28% and 82% respectively.

DISCUSSION

Chronic liver diseases with viral infection manifest varying degrees of hepatic fibrosis ranging from no fibrosis to cirrhosis. Yoshida et al revealed that the annual incidence of hepatocellular carcinoma increased from 0.5% among patients with the stage F0 or F1 fibrosis to 7.9% among the patients with stage F4 fibrosis.[10] It has thus become increasingly apparent that the fibrosis stage is a key factor in defining the prognosis and management of chronic liver diseases with a viral infection.

Diagnostic accuracy of liver cirrhosis can be evaluated by imaging modalities, including CT scan, MRI and Ultrasound, compared to results obtained from histopathological diagnosis. The gold standard in hepatology for the diagnosis of the fibrosis stage has been a histological liver evaluation based on specimens taken either by a needle biopsy or at operation. Recently, non-invasive and reliable assessments for monitoring chronic liver disease using the platelet counts[11-13], aspartate aminotransferase (AST)/alanine aminotransferase (ALT) ratio[12,13], and serum hyaluronan and type III procollagen amino-terminal peptide[14] have been developed. However, none of the currently available tests or modalities can completely replace a histological analysis. Previous studies have

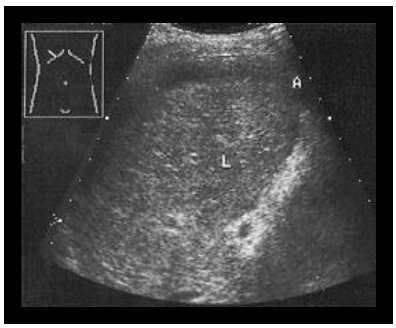

Figure .1: Ultrasound liver showed blunted liver edge, irregular surface and Coarse parenchymal texture. (Sever fibrosis)

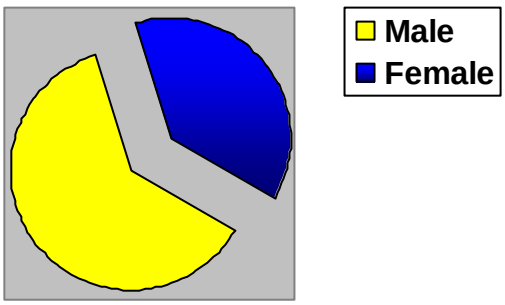

Figure 2: Gender Distribution patients (n=50).

assessed several methods for evaluating the fibrosis stage of chronic liver disease using various Ultrasound parameters. However, there have so far been few studies concerning the accuracy in detecting the signs of compensated cirrhosis by ultrasound[15,16]. Gaiani et al[15] and Hung et al[17] proposed a complex ultrasound scoring system using indices of the liver surface, parenchymal echogenicity, the vessel pattern, spleen size etc. to determine the fibrosis stage. In addition, recent advances in ultrasound technology have now made it possible to obtain more precise information about the liver surface, edge and parenchymal texture[17,18]. Therefore, we conducted this study to clarify whether the Ultrasound scoring system with a newly developed Ultrasound equipment based on the conventional parameters of the liver edge, surface and parenchymal texture might obtain sufficiently accurate results in comparison with the histological findings for fibrosis obtained by a liver biopsy.

In this study, among these parameters such as the liver edge, liver surface and liver parenchymal texture, the liver edge was not as specific for evaluating liver fibrosis as the liver surface and parenchymal texture in our study because a mildly blunted (score 1) or blunted edge (score 2) was frequently found in the early fibrosis stage (stage 1). On the other hand, the liver surface and liver parenchymal texture obtained by ultrasound showed a better comparison with the histological findings.

With conventional ultrasound, the liver surface has been most commonly utilized as a sole indicator for the diagnosis of cirrhosis[15,19]. However, numerous papers have reported that the sole factor of the liver surface can not sufficiently distinguish cirrhosis from chronic hepatitis. Gaiani et al confirmed that the stage of cirrhosis may be underestimated when based on a single specimen and clarified that only two ultrasound variables, namely liver surface nodularity and the portal vein mean flow velocity, independently contributed to the diagnosis of cirrhosis[15]. In our study, all patients with a highly irregular surface were found to have cirrhosis (stage 4-severe fibrosis) histologically. Indeed, the results of our study showed a significant comparison between the ultrasound liver fibrosis stage based upon ultrasound scoring system and the histological fibrosis stage.

An irregular and nodular liver surface may be easily assessed in patients with decompensated liver cirrhosis, particularly in the case of ascites. In our study, both the right and the left liver lobes were evaluated for scoring each factor and the accumulated score was calculated. Ultrasound was performed to determine the sensitivity and probability according to the characteristics of ultrasound. Furthermore, although the major drawback with ultrasound in comparison with the liver histology has been considered to be the failure to detect mild fibrosis or none at all, our scoring system thus provided relatively accurate information about liver fibrosis. In addition, the score proposed in our study is easy to obtain and can be applied in every ultrasound by utilizing regular commercially available ultrasound equipment.

Our scoring system based on three parameters such as the liver edge, surface and parenchymal texture was able to accurately predict the fibrosis stage especially when distinguishing chronic hepatitis from compensated liver cirrhosis. When an exclusion of liver cirrhosis is requested, then ultrasound alone is, therefore considered to provide sufficient information based on this scoring system.

Hung et al.,[20] and XU et al.,[21] revealed the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 92.5%, 77.8%, 87.5%, 86.0%, and 86.6%, respectively in their studies which corresponds to the results of our study. Our ultrasound scoring system for liver fibrosis is a reliable mean in detection of hepatic fibrosis in patients with laboratory findings of viral hepatitis.

CONCLUSION

We concluded that ultrasound being a non-invasive technique and cheaper is much better to perform for staging of liver fibrosis as compared to invasive liver biopsy. These

parameters may also be useful for providing prognostic information and also for determining the optimal therapeutic options during the follow-up of patients with chronic liver disease, especially in patients with chronic hepatitis C or B, in order to predict the occurrence of hepatocellular carcinoma. In addition, this study is called for to determine whether or not the wider use of this scoring system could apply to other forms of hepatic fibrosis such as those suffering from long-term hepatotoxic disease, congenital diseases in children and non-viral infective forms of chronic liver disease in order to obtain an improved response to therapy.

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