VALIDITY OF GRAY SCALE ULTRASONOGRAPHY IN DIAGNOSIS OF CHRONIC LIVER DISEASE OF VIRAL ETIOLOGY

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ABSTRACT

Objective: To determine validity of gray scale ultrasonography in diagnosis of chronic liver disease of viral etiology.

Study Design: Validation study.

Place and Duration of Study: Medical departments of Rawalpindi Medical College and Allied Hospitals, Rawalpindi in collaboration with Radiology and Pathology departments from 16th June 2008 to 16th Dec 2008.

Material and Methods: A sample of 75 patients with polymerase chain reaction (PCR) positive for hepatitis B and C comprising of 33 male and 42 female in the age groups of 19 to 58 years was taken for the study. The patients fulfilling the inclusion criterion were subjected to abdominal ultrasound. Later on findings were confirmed by histopathological findings. The patients were subjected to greyscale ultrasonography in the three parameters of; Edge in terms of sharp, slightly blunted edge, moderately blunted edge and grossly blunted edge; Surface on terms of smooth, slightly irregular, moderately irregular and markedly irregular; Parenchymal texture in terms of fine, slightly coarse, moderately coarse and markedly coarse. For histological examination percutaneous liver biopsy specimens were obtained from the anterior segment of the right lobe in each patient under the guidance of ultrasound. Histopathological grading was distributed over 5 category scales, i.e. "No fibrosis; Fibrosis portal expansion; Bridging fibrosis; Bridging fibrosis with lobular degeneration and Cirrhosis".

Results: Statistical analysis of the current study revealed that; overall diagnostic accuracy of ultrasound as 86.67% as comparable with gold standard biopsy. Sensitivity was found to be 92.98 %, and Specificity 66.67 %. Positive predictive value was 89.83% and negative predictive value was 75.0% in comparison with gold standard of liver biopsy.

Conclusion: The study concludes that ultrasound is equally reliable and dependable technique for the diagnosis of chronic liver disease of viral etiology as compared to histopathological grading.

Keywords: Cirrhosis, Fibrosis stage, Histopathological Grading, Ultrasonography, Viral Hepatitis.

INTRODUCTION

Viral hepatitis is a major public health problem globally. Nearly 1% to 3% of the people in developed world are chronically infected with hepatitis C-virus while carriage rate in other countries is reaching up to 35%[1]. The burden of hepatitis C virus (HCV) related chronic liver disease in Pakistan has increased over the years. Recent data shows nearly 60 to 70% patients with chronic liver disease tend to be positive for anti-HCV. It has been demonstrated that nearly 50% patients with hepato- cellular carcinoma in Pakistan are HCV positive[2]. Hepatitis B causes an estimated 1 to 2 million deaths per year and there are three hundred million carriers of hapatitis B virus (HBV) in the world. Accurate estimation of the disease severity is helpful for the evaluation of the therapeutic effect and the prognosis of the disease. At present there are various modalities for this purpose, these including histology, serology, and imaging[3]. Liver biopsy remains the only accepted test for staging and grading of chronic liver disease of viral etiology. However this procedure is associated with significant

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patient morbity and a small but definite risk of death[1]. On the contrary sonography is still the most established, risk free method for diagnosis and follow up of chronic viral hepatitis[4-5] primarily because of its low cost, easy performance and high acceptability for the patient[3]. An ultrasound evaluation of the liver fibrosis stage of chronic liver disease has been performed by assessing various ultrasound factors such as liver size, the bluntness of the liver edge, the coarseness of the liver parenchyma, nodularity of the liver surface, the size of the lymph nodes around the hepatic artery ,the irregularity and narrowness of inferior vena cava, portal vein velocity or spleen size[5-6].

Therefore this study has been conducted to evaluate the accuracy of liver fibrosis stage by ultrasonography and compared with histopathological findings. The primary aim of this work was to evaluate the validity of grey scale ultrasonography in assessing diagnosis and progression of chronic viral hepatitis in patients with chronic liver disease. Ultrasonography is a non-invasive and comparatively less expensive procedure with high patient acceptance. If it has an established acceptable diagnostic validity, it can be used in place of liver biopsies or polymerase chain reaction (PCR).

MATERIAL AND METHODS

It was the validation study conducted in the Medical departments of Rawalpindi Medical College and Allied Hospitals Rawalpindi in collaboration with Radiology and Pathology departments from 16th June 2008 to 16th Dec 2008. History of chronic liver disease based on the detection of persistently raised levels of alanine transferase (ALT) and positive PCR were the inclusion criteria. Exclusion criteria were patients with extreme of ages, patients who had a previous histopathology diagnosis and patients who were on interferon therapy. A sample of 75 patients with PCR positive for hepatitis B & C were included in the study. The patients were subjected to greyscale ultrasonography in the three parameters of; Edge in terms of sharp, slightly blunted edge, moderately blunted edge and grossly blunted edge; Surface on terms of smooth, slightly irregular, moderately irregular and markedly irregular; Parenchymal texture in terms of fine, slightly coarse, moderately coarse and markedly coarse. All scans were carried out using ALOKA Pro-sound 4000 SSD machine. The procedure was carried out using a 3.5MHz convex curvilinear transducer and observation were made according to the ultrasound score system. For histological examination percutaneous liver biopsy specimens were obtained from the anterior segment of the right lobe in each patient under the guidance of ultrasound. Histopathological grading was distributed over 5 category scales, i.e. "No fibrosis; Fibrosis portal expansion; Bridging fibrosis; Bridging fibrosis with lobular

Table-1: Cross tabulation of ultrasonography and histopathology (n=75).

		Ultrasonography	
Histopathology	**Cirrhosis**	Fibrosis	No fibrosis
		True positive	False Positive
		53	06
	No cirrhosis	False negative	True negative
		04	12

Table-2: Diagnostic accuracy of gray scale ultrasonography.

Diagnostic accuracy	**Percentage**
Sensitivity	92.98 %
Specificity	66.67 %
Positive predictive value	89.83 %
Negative predictive value	75.0 %
Diagnostic accuracy	86.67 %

degeneration and Cirrhosis". An experienced histopathologist without any knowledge of the clinical details and the ultrasound findings reviewed all the slides. The results were compared with histopathology grading for 'no fibrosis to cirrhosis' over a period of six months.

Data were stored and analyzed by SPSS version 13.0. Sensitivity specificity, Positive predictive value (PPV) and Negative predictive value (NPV) of ultrasound were calculated taking histopathological findings as gold standard. Frequencies and percentages were calculated for various ultrasound findings. A 2x2 table-1 was used to associate the results of grayscale ultrasonography with histopathology.

RESULTS

A total number of 75 patients were included in this study. Of the total 75 patients, 42 (56%) were female and 33 (44%) were male between the age group of 19 to 58 years with the mean age of 34 years. No patient was lost or dropped from the study. All these patients assessed in the three standard parameters of grayscale ultrasound. Results for the ultrasound edge, ultrasound surface and ultrasound parenchymal indicating that 50.6% of patients with blunted edge, and 52.1% having markedly irregular surface and 49.3% patients with markedly coarse parenchyma.

The results were compared and revealed that for a sample size of 75, 53 patients having fibrosis fall closely to the 52 patients reported to have proven cirrhosis. The study therefore established a close association between the results of ultrasound indices and that of histopathological grading. Thus the validity of gray scale ultrasonography in diagnosis of chronic liver disease is established.

Statistical analysis of the current study revealed that; overall diagnostic accuracy of ultrasound as 86.67% as comparable with gold standard biopsy. Sensitivity was found to be 92.98%, and specificity 66.67%. Positive predictive value was 89.83% and negative predictive value was 75.0%.

DISCUSSION

The aim of this work was to determine diagnostic validity of grayscale ultrasonography in chronic liver disease of viral etiology keeping gold standard as histopathology. Ultrasonography is a non-invasive and comparatively less expensive procedure. An attempt was made through this study to find out an acceptable diagnostic accuracy, so that the grey scale ultrasonography could be used in place of liver biopsies or PCR

Various gray scale ultrasound parameters have been evaluated and compared with

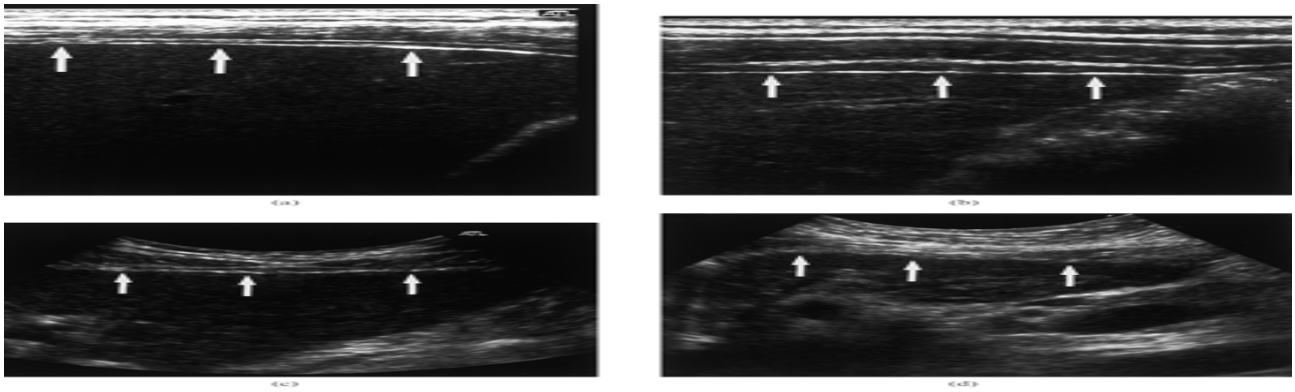

Figure-1: Ultrasound Images.

Image: Scores for the ultrasound features of the liver parenchymal texture; (a) Fine parenchymal texture, (b) A mildly coarse parenchymal texture, (c) A coarse parenchymal texture probe, (d) a highly coarse parenchymal texture

histopathology as a single ultrasound parameter is limited in sensitivity and specificity for diagnosis of early cirrhosis, as stated by Shen et al[15]. Of the total 75 patients, 42(56%) were female and 33(44%) were male between the age group of 19 to 58 years with the mean age of study population as 34 years as a comparable sample. A study conducted by Nishiura et al[14] determined fibrosis stage in chronic liver disease in 103 patients (60 male and 43 female patients) with a percentage of 58% and 42% respectively, which is closer to the current study.

The study conducted by Nishiura et al[14] reported mean age of the patients as 51 years implying a comparatively an older age sampled population against 34 years as mean age being reported by the current study. These results reflect hepatitis B and C affects people in developing countries like Pakistan comparatively at a younger age than elsewhere as also supported by Hameed S et al[21].

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 4 fibrosis[16]. 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.

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[13,14] aspartate aminotransferase (AST)/alanine aminotransferase (ALT) ratio[13] and serum hyaluronan and type III procollagen amino-terminal peptide[9] have been developed. However, none of the currently available tests or modalities can completely replace a histological analysis. Previous studies have 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 US. Gaiani et al[10] and Hung et al[22] proposed a complex ultrasound scoring system using indices of the liver surface, parenchymal echogenecity, 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. Therefore, this study has been conducted 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.

With conventional ultrasound, the liver surface has been most commonly utilized as a sole indicator for the diagnosis of cirrhosis [6,13], 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

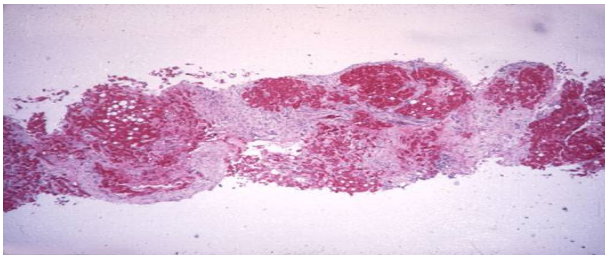

Figure-2: Photomicrograph showing cirrhosis of liverImage.

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[10].

Previous studies have 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[11,12].

Gaiani et al[10] and Hung et al[22] proposed a complex ultrasound scoring system using indices of the liver surface, parenchymal echogenecity, 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[13]. The current study therefore validated the ultrasound scoring system with newly developed US equipment based on the conventional parameters of the liver edge, surface and parenchymal texture and thus obtained sufficiently accurate results in comparison with the histological findings for fibrosis obtained a liver biopsy, as presented in table-1.

Although this study was limited on account of the relatively small number of patients due to the strict inclusion criteria, 53 patients were found to have a fibrosis score of 4. Therefore, the scoring system for predicting cirrhosis was found to be 92.98% sensitive. A major drawback with ultrasound in comparison with the liver histology has been considered to be its failure to detect mild fibrosis or none at all. This is however considered a valid limitation with ultrasound application, which might otherwise be supplemented with histopathological technique in rare cases.

Evaluating the ultrasound pattern using either one or two parameters becomes much more complex at the stage of chronic liver disease than that of complete cirrhosis. The current study having scoring system based on three parameters such as the liver edge, surface and parenchymal texture was able to accurately predict the fibrosis stage. When an exclusion of liver cirrhosis is requested, then ultrasound alone is therefore considered to provide sufficient information based on this scoring system as validated in the current study. Furthermore, if a histological analysis cannot determine the fibrosis stage correctly due to fragmentation or architectural distortion, then this ultrasound diagnostic modality of fibrosis could replace a histological diagnosis, per se.

On the basis of results obtained from this research, the current study concludes that ultrasound is equally a very reliable, comparable and dependable technique for the validation of grayscale ultrasonography in diagnosis of chronic liver disease of viral etiology as compared to histopathological grading.

CONCLUSION

The study concludes that ultrasound is equally a reliable, comparable and dependable technique for the validation of grey scale ultrasonography in diagnosis of chronic liver disease of viral etiology as histopathological grading.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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