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Comparative analysis of Shear Wave Elastography with serological indices for diagnosis of liver fibrosis in a tertiary care hospital in Pakistan

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Hepatic parenchyma disorders are prevalent in contemporary life. These illnesses include chronic liver disease and liver fibrosis etc. Shear Wave Elastography is a novel technique that was created based on the application of shear waves and is used for diagnosis of these diseases. Serum-based biomarkers i.e., APRI and Fib-4 have been extensively researched and are established in clinical practice. This study aims to assess the diagnostic efficiency of SWE with APRI and FIB-4, in identifying the degree of liver fibrosis. Study Design: Retrospective Cross-Sectional Study This study was conducted at the Radiology Department of Quaid e Azam International Hospital, Islamabad from 01st March 2022 to 01st March 2023. A total of 60 patients were enrolled in this study. Fibrosis was defined on SWE. The serum concentrations of APRI and Fib-4 were noted. Data was analyzed in SPSS version 26.The mean age of the patients enrolled in the study was 44.050 ± 14.65 ($p<0.001$). The area under the curve (AUC) for SWE as compared to APRI was 0.772 and as compared to FIB-4 was 0.741. The sensitivity and specificity as compared to APRI was 64.4% and 80% respectively and as compared to FIB-4 was 69.2% and this 76.2%.The diagnostic accuracy of SWE was comparable to FIB-4 and APRI. The sensitivity, specificity and AUC value of SWE was quite similar to values of FIB-4 and APRI in reported literature. Therefore, SWE can serve as a suitable alternative for liver fibrosis detection and classification.

Keywords: Cirrhosis, Hepatic parenchymal disorders, SWE, APRI, FIB-4, ROC, AUC

INTRODUCTION

Hepatic parenchyma disorders are fairly prevalent in contemporary life and present in a variety of ways. These illnesses include chronic liver disease, which is nearly always brought on by viral infections, and nonalcoholic fatty liver disease (Cheemerla and Balakrishnan, 2021; Cotter and Rinella, 2020). All of these conditions that affect the parenchyma of the liver, however, virtually inevitably lead to cirrhosis (Garrido and Djouder, 2021). An early management strategy must be created because fatty liver, nonalcoholic fatty liver disease (NAFLD), and chronic liver disease (CLD) are all stages of the same illness.

The "gold standard" method for detecting liver problems including fibrosis and cirrhosis historically used a liver biopsy (Berger et al. 2019). The value of biopsy has been surpassed by more recent diagnostic techniques. Liver histology grading systems are used to assess the architecture and fibrosis of the liver. As a result of how intrusive it is, researchers are looking for noninvasive ways to assess the stages of liver fibrosis (Heyens et al. 2021; Berger et al. 2019).Non-invasive liver diagnostics encompass imaging modalities, direct serum markers, and indirect serum indicators (Liaqat et al. 2021). The imaging method most usually used is transient elastography, also referred to as Fibro scan. Because it is less invasive and more secure than a biopsy, it can be used in place of that procedure. SWE is a novel technique that was created based on the application of shear waves to a diagnostic ultrasound

system (Davis et al. 2019).

The health care systems of low- and middle-income countries often struggle with the adoption of sophisticated medical equipment due to low availability and improper allocation of budget (Fazal et al. 2022). Pakistan is no exception and has a low rate of SWE adoption because the healthcare system of Pakistan is still developing and adoption of SWE imaging modalities is often not feasible in many of its remote areas (Liaqat et al. 2021). There aren't many studies showing the SWE's usefulness, safety, and success to varied degrees in Pakistan and therefore, there is a need to assess the SWE diagnostic ability in the local Pakistani population.

This study aims to assess the diagnostic efficiency of SWE with two non-invasive markers, namely APRI and FIB-4, in identifying the degree of liver fibrosis in individuals with varying presentations of hepatic parenchymal disease.

MATERIALS AND METHODS

This study was conducted at the Radiology Department of Quaid e Azam International Hospital, Islamabad from 01st March 2022 to 01st March 2023. A total of 60 patients were enrolled in this study in a retrospective manner. The study was approved from the Institutional Review Board Committee of Quaid e Azam International Hospital, Islamabad. Consent was obtained from all participants prior to enrollment in this study. Samples were collected according to a strict inclusion and exclusion criteria as follows.

Inclusion criteria:

All patients with clinical suspicion of hepatic parenchymal disease (Fatty liver, -any grade, chronic liver disease, cirrhosis) who were referred to the Radiology Dept for the SWE were included in the study irrespective of gender and age.

Exclusion criteria:

Patients with liver lesions, ascites, pleural effusion were excluded from the study.

Patients who fulfilled the selection criteria were included in this study. Enrolled patients underwent ultrasound shear wave elastography (SWE). The demographic details were recorded on a preset proforma including patient's age and gender as well as their fibrosis score on SWE. Serum levels of Fib-4 and APRI were determined via lab tests.

SPSS version 26 was used for analysis of data. Frequency and percentage were used for qualitative variables. Mean and standard deviation were computed via independent t-test analysis for the quantitative variables. Diagnostic accuracy of shear wave elastography was assessed via ROC curve analysis. For the purpose of ROC curve analysis, patients with F1 and F2 fibrosis were grouped together comprising significant fibrosis. Stages F3 and F4 were also grouped together comprising advanced fibrosis or cirrhosis.

RESULTS

Descriptive variables i.e., Age and Gender are presented in Table 1 in terms of frequency (gender) and mean (age). The mean age of the patients enrolled in the study was 44.050 ± 14.65 ($p<0.001$). 65% of the study population was male as compared to 35% as females.

Table 1; Analysis of descriptive variables in terms of Frequency and percentage (Gender) and mean ± SD (Age)

Variable	Groups	Frequency	Percentage
Gender	**Male**	39	65%
	Female	21	35%
	Total	60	100
Age	44.050 ± 14.65 ($p<0.001$)		

Serum marker levels of APRI and FIB-4 obtained from the patients were analyzed in terms of descriptive analysis as shown in Table 2. The mean of APRI was 0.662 ± 0.815 ($p<0.001$), whereas the mean of FIB-4 was determined as 1.66 ± 2.20 ($p<0.001$).

Table 2: Descriptive statistics for serum markers of Chronic Liver Disease patients

Variable	Minimum	Maximum	Mean ± SD
APRI	0.11	5.79	0.662 ± 0.815 ($p<0.001$)
FIB-4	0.27	15.73	1.66 ± 2.20 ($p<0.001$)

The frequency and percentage of shear wave elastography evaluation of enrolled patients is shown in Table 3. 53.3% of the patients were diagnosed with F0-F1 stage, followed by 28.3% in F2, 3.3% in F3 and lastly 15% as F4.

Table 3: Frequency and percentage of Shear wave Elastography analysis of all patients enrolled in the study.

Variable	Stage	Frequency	Percentage
Shear Wave Elastography	F0-F1	32	53.3%
	F2	17	28.3%
	F3	2	3.3%
	F4	9	15%
	Total	60	100

The diagnostic ability of shear wave elastography was measured with ROC curve analysis. The ROC curve obtained for SWE in relation to APRI is shown in Figure 1. The cut off values of APRI and FIB-4 for diagnosis of F1/F2 and F3/F4 stage fibrosis were obtained from previous literature (Papadopoulos *et al.* 2019). The

diagnosis was divided as significant fibrosis F1/F2, followed by cirrhosis (F3/F4 fibrosis). The area under the curve (AUC) was determined as 0.772. The sensitivity was determined as 64.4% and specificity as 80%.

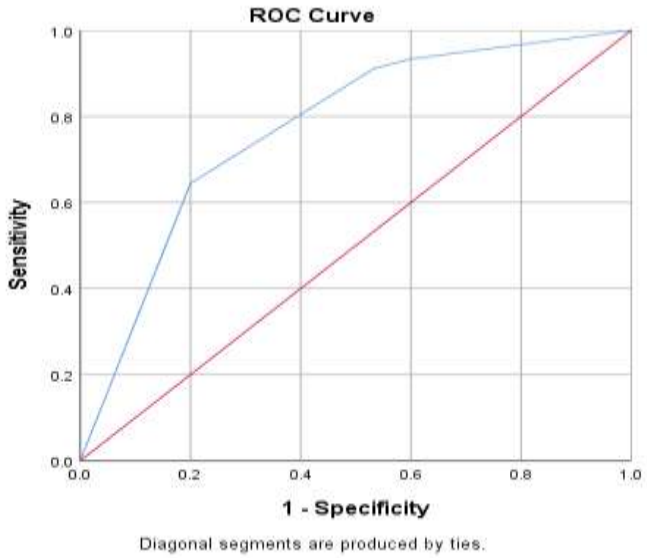

Figure 1: ROC curve analysis of SWE in relation to APRI diagnosis of fibrosis stages (AUC=0.772)

The ROC curve obtained for SWE in relation to FIB-4 is shown in Figure 2. The area under the curve (AUC) was determined as 0.741. The sensitivity was determined as 69.2% whereas the specificity was obtained as 76.2%

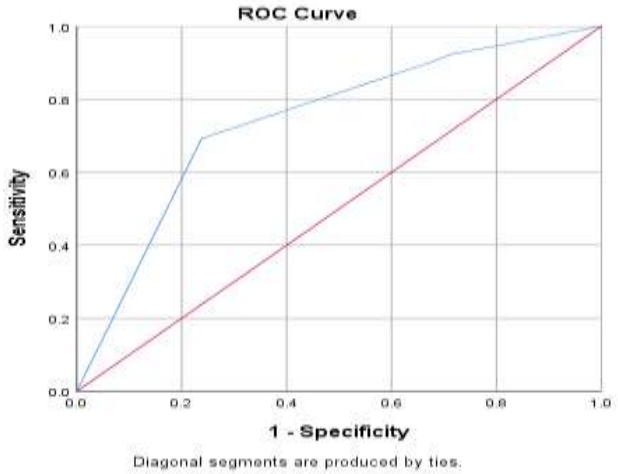

Figure 2 ROC curve analysis of FIB-4 in relation to SWE F4 fibrosis (AUC= 0.741)

DISCUSSION

The purpose of this study was to investigate the capability of shear wave elastography for diagnosis of liver fibrosis and its classification into stages and their comparison with the results of serum biomarkers APRI and FIB-4 in patients with variable presentation of hepatic parenchymal disease. According to the results of this study, SWE possesses good diagnostic potential of liver fibrosis and its classification into different stages. The results are comparable to the sensitivity and specificity recorded for APRI and FIB-4 in previous studies.

These are promising results as shear wave elastography is generally not very much in practice in multiple parts of the world mainly the Low- and Middle-Income Countries (LMIC) (Liaqat et al. 2021; Manzoor et al. 2018). In a systematic review published in 2021, AUC for prognosis of liver diseases ranged from 0.71 to 0.89 for FIB-4 and 0.69-0.89 for APRI (Lee et al. 2021). This systematic review compiling recent research is all in accordance with our AUC observed values for SWE. Another recent meta-analysis also revealed that the AUROCs for both APRI and FIB-4 for detection of liver fibrosis at an early, intermediate and advanced stage were 0.76 and 0.75, 0.74 and 0.77, and 0.77 and 0.82, respectively (Dong et al. 2021).

Recent literature has also indicated that when compared to liver fibrosis, SWE possesses better sensitivity and specificity as compared to serum diagnosis via biomarkers. Tada et al. showed that the area under the curve for SWE was greater in comparison to APRI and FIB-4 in diagnosis and classification of liver fibrosis (Tada et al. 2015). Similar observation was made with diagnosis of substantial fibrosis (F1/F2), severe fibrosis (F3/F4) in another study which found that the SWE's ability to diagnose and classify fibrosis was significantly higher ($p<0.005$) (Zhuang et al. 2016).

However, there are studies which also indicate very high utility of APRI and FIB-4 in diagnosis of fibrosis. One study conducted in India predicted similar diagnostic parameters for chronic hepatitis C patients. They found that in predicting fibrosis in untreated chronic hepatitis C patients, APRI and FIB-4 demonstrated diagnostic accuracies of 84.29%, 81.43% (mild fibrosis), 78.95%, 92.11% (moderate fibrosis), and 73.68%, 73.68% (severe fibrosis), respectively (Kiran Kujur et al. 2020).

The high variability in results of serum-based diagnosis of fibrosis requires a solid alternative. The WHO guidelines find limited utility of biomarkers for diagnosis of fibrosis stages with a clear indication of no clinical utility of FIB-4 for F3 and F4 stages of fibrosis (Rungta et al. 2021). Shear wave elastography can provide a suitable, minimally invasive method for the diagnosis and further classification of SWE.

CONCLUSIONS

In terms of diagnosis of liver fibrosis, the diagnostic accuracy of SWE was found comparable to the commonly used serological indices i.e., FIB-4 and APRI. The diagnostic parameters i.e., the sensitivity, specificity

and AUC value of SWE was quite similar to values of FIB-4 and APRI reported in literature. Therefore, SWE can serve as a suitable alternative for liver fibrosis detection and classification.

Supplementary materials
Not applicable

Author contributions
All authors have contributed in this research equally

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Institutional Review Board Statement
The study was approved by the Institutional Review Board Committee of the Quaid e Azam International Hospital, Islamabad.

Informed Consent Statement
The study was performed in accordance with relevant institutional and national guidelines, with the appropriate institutional ethics committee's prior approval and informed written consent from all human subjects involved in the study including for publication of the results.

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Conflict of interest
The authors declare no conflict of interest.

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