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ORIGINAL ARTICLE

Comparison of Shearwave Elastography and Apri Score for Liver Fibrosis in Patients of Chronic Liver Disease

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ABSTRACT

Chronic liver disease of various etiologies is the major causes of mortality and morbidity globally. Liver biopsy is the most accurate and oldest method to determine the chronic liver disease progression and for liver histology. Shear wave elastography (SWE) is a new non-invasive technique that applies localized mechanical compression to the soft tissue with focused ultrasonography and obtains tension images showing the tissue response. Aspartate aminotransferase to platelets ratio (APRI) on the other hand is relatively less expensive test and can be done on outpatient basis.

Objective: To find the relation between APRI aspartate and SWE for detection of liver fibrosis in patients with chronic liver disease.

Study Design: A Cross Sectional study

Setting: Medical Unit-1 Lahore General Hospital Lahore and Department of Gastroenterology & Hepatology, Doctors Hospital and Medical Centre, Lahore.

Study Duration: From July 2019 to December 2021.

Methods: 180 patients met the criteria of inclusion were included, the blood samples were obtained and sent to the hospital laboratory for valuation of AST and Platelets. Reports were evaluated, APRI was calculated and patients were labeled as negative or positive. Then all patients underwent SWE by a senior radiologist for assessment of liver fibrosis. Patients were labeled as negative or positive. Agreement was noted, all data was entered on a specifically designed proforma, and data were analyzed and entered in SPSS version 20 statistical method. Agreement was calculated by generating 2x2 tables between APRI and SWE findings. Kappa statistics was calculated to measure the strength and significance of agreement. P-value ≤0.05 was taken as significant.

Results: In this study, the patients mean age was 46.39 ± 16.02years. There were 119 (66.11%) males and 61 (33.89%) females. The mean BMI of patients was 24.70 ± 5.23kg/m^2. The mean duration of CLD was 5.50 ± 2.672 years. The mean AST of patients was 73.98 ± 60.23IU/L while mean platelet count was 200.65 ± 92.47/cm^3. The mean APRI was 1.41 ± 1.20. The mean SWE was 18.32 ± 23.85kPa. The APRI and SWE agreed on 73 (54.9%) cases and showed 66.7% agreement between them for diagnosis of liver fibrosis ($p<0.05$).

Conclusion: Thus, APRI and SWE showed strong agreement but further trials are required to confirm the evidence.

Keywords: Agreement, APRI, Aspartate aminotransferase to platelets ratio, SWE, Shear-wave elastography, Chronic liver disease and Liver fibrosis.

INTRODUCTION

Chronic liver disease due to various causing factors is the major causes of mortality and morbidity globally. CLD progressesion is through various pathological stages, from mild hepatitis lacking fibrosis to advanced cirrhosis and fibrosis. Hepatitis B and C are the communal causes of hepatocellular carcinoma and cirrhosis worldwide. More than 3% of the population in the world, or almost 17 billion individuals, may have hepatitis C virus (HCV). In Pakistan, the incidence of liver fibrosis among cases with HCV or HBV is 53.1%.

Liver biopsy is the most accurate and oldest method to determine the chronic liver disease progression and for liver histology. There are risks of complications after a liver biopsy, which can range from minor symptoms, like mild pain in the abdomen, to severe bleeding and the bile ducts injury. Due to the complications risk, some patients may refuse a liver biopsy. Shear wave elastography (SWE) is a new non-invasive technique that applies localized mechanical pressure to soft tissue using focused ultrasonography and obtains strain images showing the response of the tissue.

One study conducted on aspartate aminotransferase to platelets ratio (APRI) for fibrosis of liver assessment showed that the sensitivity of APRI was 41-91% and specificity 47-95%.[11] Another study showed that the sensitivity of APRI was 89% and specificity 75%.[1] Further studies showed that the sensitivity of APRI was 42.9% and specificity 85.4%.[12]

Sande JA, Verjee S, Vinayak S, et al reported, that APRI along with SWE, showed AUC (area under curve) equal to 0.920, which showed 92% agreement between APRI and SWE for liver fibrosis analysis.[13]

This study goal is to determine the agreement between APRI and SWE for liver fibrosis anlaysis in patients comparing with SWE. SWE is an expensive procedure and also requires expertise; moreover, SWE is not readily available in all settings. APRI on the other hand is relatively less expensive test and readily available.

Therefore, we wish to compare the two above mentioned tests i.e., SWE and APRI for detection of liver fibrosis and wish to get the measure of agreement between APRI and SWE to take the advantage of cheaper APRI, if agreement was found between both. There is no local data to compare these modalities, for cost effectiveness.

METHODS

This Cross-sectional study was held in the Medical Unit-1 Lahore General Hospital, Lahore and Department of Gastroenterology & Hepatology, Doctors Hospital and Medical Centre, Lahore from July 2019 to December 2021. Sample size of 180 cases is calculated with confidence level of 95%, marginal error of 4% and taking expected percentage i.e., 92% between APRI and SWE for detection of liver fibrosis. Non-probability, consecutive sampling technique was used for patients' selection.

Inclusion Criteria:

- Age 20-70 years of either gender
- All Patients with HCV or HBV presenting with chronic liver disease for at least 6months duration

Exclusion Criteria:

- Hepatocellular carcinoma (on medical record).
- Portal vein and Hepatic vein thrombosis diagnosed on Doppler
- Congestive cardiac failure (on medical record)

- Pregnancy

180 patients fulfilled the inclusion criteria were selected from the inpatient and Outpatient Medical Unit-1 Lahore General Hospital Lahore and Department of Gastroenterology, Doctors Hospital and Medical Centre, Lahore. The purpose of the study was explained to each patient and informed consent was attained. Demographic data counting age, name, BMI, gender, cirrhosis duration was also obtained. Then blood sample was taken by using 3cc BD syringe under aseptic measures. Blood was stored in vials containing ethylenediaminetetraacetic acid solution to prevent clotting. All samples were sent to the hospital laboratory for valuation of AST and Platelets. Reports were evaluated and levels were noted. APRI was calculated and patients were labelled as positive or negative (as per operational definition). Then all patients underwent SWE by a senior radiologist for assessment of liver fibrosis. Patients were labelled as positive or negative. All the data was entered on a specially designed proforma.

Data were analyzed and entered in SPSS version 20. Quantitative variables i.e., age and BMI were accessible as mean and SD. Categorical variables i.e., gender and liver fibrosis (on APRI & SWE) were presented as frequency and percentage. 2x2 tables between APRI and SWE findings were calculated. To measure the strength and significance of agreement Kappa statistics was applied. The stratification of data was done for gender, age, BMI of patient and duration of CLD. Agreement was calculated by generating 2x2 tables between APRI and SWE findings. To measure the strength Kappa statistics was calculated and significance of agreement for each stratum. P-value ≤0.05 was taken as significant.

RESULTS

In this study, the mean age of patients was 46.39 ± 16.02years. Table 1

Table 1: shows the descriptive Statistics of Age of patients

Age (years)	n	180
	Mean	46.39
	SD	16.02
	Minimum	20
	Maximum	70

There were 119 (66.11%) males and 61 (33.89%) females. Fig 1

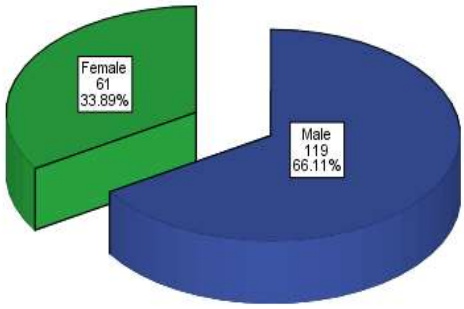

Table-2: shows the Descriptive Statistics of BMI patients and duration of CLD

BMI (kg/m^2)	n	180
	Mean	24.70
	SD	5.23
	Minimum	16.20
	Maximum	34.93
Duration (years)	n	180
	Mean	5.50
	SD	2.67
	Minimum	1
	Maximum	10

The mean BMI of patients was 24.70 ± 5.23kg/m^2. The mean duration of CLD was 5.50 ± 2.672years.

Table 3: shows the Descriptive Statistics of AST and platelet count and APRI of patients

		AST	Platelet count
n		180	180
Mean		73.98	200.65
SD		60.23	92.47
Minimum		22	58
Maximum		225	367
APRI	n	180	
	Mean	1.41	
	SD	1.20	
	Minimum	0.19	
	Maximum	5.12	

The mean AST of patients was 73.98 ± 60.23IU/L while mean platelet count was 200.65 ± 92.47/cm^3. The mean APRI was 1.41 ± 1.20.

The mean SWE was 18.32 ± 23.85kPa. Table 4

Table 4: shows the Descriptive Statistics of SWE

SWE (kPa)	n	180
	Mean	18.32
	SD	23.85
	Minimum	5.80
	Maximum	129.30

On SWE, liver fibrosis was predicted positive in 133 (73.89%) cases while 47 (26.11%) were negative. Fig 3

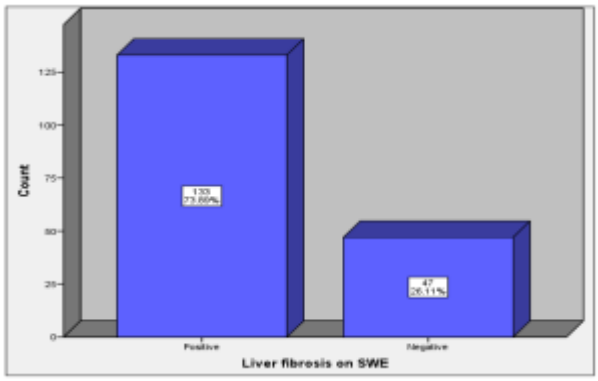

Fig 2: shows the Distribution of Liver fibrosis on SWE

Table 5: shows the Distribution of Agreement between APRI & SWE

		Liver fibrosis on SWE		Total
		Positive	Negative	
Liver fibrosis on APRI	Positive	73	0	73
		54.9%	0.0%	40.6%
	Negative	60	47	107
		45.1%	100%	59.4%
Total		133	47	180
		100%	100%	100%

DISCUSSION

The degree of fibrosis of liver are crucial for making treatment choices and predicting clinical results. Presently, liver biopsy is considered as the reference standard for the assessment of liver fibrosis is being questioned due to the growing awareness of a number of disadvantages (invasiveness, sampling bias, inter-observation variability) associated with its use. In parallel, in recent years there has been a rapid increase in the non-invasive evaluation of fibrosis of liver and a wide variety of non-invasive techniques have been established, from serum analysis to imaging techniques. Some of them, such as Fibrosure/ Fibrotest and in Europe, transient elastography are approved methods acquiring acceptance in clinical practice, particularly in chronic hepatitis C.

Large-scale authentication in the context of other diseases of choric liver is awaited. Though, the non-invasive tests used to perceive the two main clinical endpoints, significant fibrosis and cirrhosis, still do not perform well in routine diagnostic testing and there is still no ideal substitute or replacement for the optimal method of liver biopsy. In our study, the mean AST of patients was 73.98 ± 60.23IU/L while mean platelet count was 200.65 ± 92.47/cm3. The mean APRI was 1.41 ± 1.20. On APRI, liver fibrosis was predicted positive in 73 (40.56%) cases while 107 (59.44%) were negative. In our study, the mean SWE was 18.32 ± 23.85kPa. On SWE, liver fibrosis was predicted positive in 133 (73.89%) cases while 47 (26.11%) were negative. Thus, the APRI and SWE agreed on 73 (54.9%) cases. Thus; this showed 66.7% agreement between them for diagnosis of liver fibrosis. The agreement was significant (kappa; p-value<0.05).

One study conducted on APRI for assessment of liver fibrosis showed that the sensitivity of APRI was 41-91% and specificity 47-95%. Another study showed that the sensitivity of APRI was 89% and specificity 75%. Further studies showed that the sensitivity of APRI was 42.9% and specificity 85.4%.

Sande JA, Verjee S, Vinayak S, et al reported, that APRI along with SWE, showed AUC (area under curve) equal to 0.920, which showed 92% agreement between APRI and SWE for detection of liver fibrosis.

In a review, it has been reported that agreement between APRI and SWE for liver fibrosis was ranged between 64-92%. Sebastiani et al., found that agreement between APRI and SWE for liver fibrosis was 72%.

In this study, the patients mean age was 46.40 ± 15.94years. Data was stratified for age of patients. In patients aged 20-45years, the agreement between APRI & SWE was 67.7% for diagnosis of liver fibrosis. In patients aged 46-70years, the agreement between APRI & SWE was 65.3% for diagnosis of liver fibrosis. The difference was insignificant (p>0.05). There were 90 (64.29%) males and 50 (35.71%) females. Data was stratified for gender of patients. In male patients aged, the agreement between APRI & SWE was 67.8% for diagnosis of liver fibrosis. In female patients, the agreement between APRI & SWE was 64.0% for diagnosis of liver fibrosis. The difference was insignificant (p>0.05).

The mean BMI of patients was 24.87 ± 5.18kg/m2. Data was stratified for BMI of patients. In underweight patients, the agreement between APRI & SWE was 90% for diagnosis of liver fibrosis. In normal weight patients, the agreement between APRI & SWE was 57.7% for liver fibrosis diagnosis. In overweight patients, the agreement between APRI & SWE was 57.5% for liver fibrosis diagnosis. In obese subjects, the agreement between APRI & SWE was 78.6% for diagnosis of liver fibrosis. The difference was significant (p<0.05).

The APRI exhibited 50% specificity and 81% sensitivity in forecasting severe fibrosis (Metavir F2), according to a 2007 meta-analysis. The specificity and sensitivity in forecasting cirrhosis with a cutoff value of 1 were 76% and 71%, respectively. The characteristic values for severe fibrosis (F2 or above), severe fibrosis (F3-F4), and cirrhosis (F4) were 0.78, 0.80, and 0.84, correspondingly, in a meta-analysis of approximately 8,700 subjects, the summary of areas covered by the APRI recipients' research. With a cutoff value of 1.0, the specificity and sensitivity values for fibrosis F2 or larger than the APRI 0.7 threshold were 72% and 77% as well as 64% and 61%, respectively.

The 1.0 APRI threshold has 76% and 72% sensitivity and specificity for cirrhosis, respectively. According to this results, APRI's diagnostic accuracy for fibrosis linked to chronic hepatitis C is only moderate, which is insufficient for a standard diagnostic procedure.

In the context of NAFLD, it has also been demonstrated to be reliable; when a cutoff value of 1.3 was employed, the specificity and sensitivity of forecasting advanced fibrosis (F3-F4) were 65-71% and 74-85%, correspondingly, and 98% and 34% utilising the FIB-4 threshold of 2.67.

The Lok Index, which incorporates the platelet count, AST/ALT and INR ratio, is an enhanced version of the APRI. With values between these cut-off points being regarded as indeterminate, this index uses two cut-off values: 0.5 to confirm cirrhosis and 0.2 to determine the liver cirrhosis. The first publication documented recipient test features of less than 0.78–0.81 for diagnosing cirrhosis in a cohort analysis of 1,141 patients with chronic hepatitis C and came to the conclusion that the model might avoid liver biopsy in fifty percent of cases. Another trial produced comparable results, although there was no clear advantage over APRI. This indicator can be used to identify cirrhosis, although its applicability may be constrained by variations in INR measurement between laboratories.

CONCLUSION

Thus, APRI and SWE showed strong agreement but further trials are required to confirm the evidence. SWE is an expensive procedure and also requires expertise; moreover, SWE is not readily available in all settings. APRI on the other hand is relatively less expensive test and can be done on outpatient basis. Now it is found that they have strong agreement between APRI and SWE. But need further trials. And for future, we will implement APRI for prediction of liver fibrosis.

REFERENCES

1. Baranova A, Lal P, Birerdinc A, Younossi ZM. Non-invasive markers for hepatic fibrosis. BMC gastroenterology 2011;11(1):1.
2 Nelson PK, Mathers BM, Cowie B, Hagan H, Des Jarlais D, Horyniak D, et al. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. The Lancet 2011;378(9791):571-83.
3 Mohd Hanafiah K, Groeger J, Flaxman AD, Wiersma ST. Global epidemiology of hepatitis C virus infection: New estimates of age-specific antibody to HCV seroprevalence. Hepatology 2013;57(4):1333-42.
4 Shaikh S, Sadik M, Hussain BG. Frequency of steatosis and its relation with the grade of fibrosis in patients with hepatitis C. Pak J Med Sci April-June 2009;25(2):283-8.
5 Jarčuška P, Janičko M, Veselíny E, Jarčuška P, Skladaný Ľ. Circulating markers of liver fibrosis progression. Clinica Chimica Acta 2010;411(15):1009-17.
6 Chalasani N, Younossi Z, Lavine JE, Diehl AM, Brunt EM, Cusi K, et al. The diagnosis and management of non-alcoholic fatty liver disease: Practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. Hepatology 2012;55(6):2005-23.
7 Ferraioli G, Tinelli C, Dal Bello B, Zicchetti M, Filice G, Filice C. Accuracy of real-time shear wave elastography for assessing liver fibrosis in chronic hepatitis C: A pilot study. Hepatology 2012;56(6):2125-33.
8 Joka D, Wahl K, Moeller S, Schlue J, Vaske B, Bahr MJ, et al. Prospective biopsy-controlled evaluation of cell death biomarkers for prediction of liver fibrosis and nonalcoholic steatohepatitis. Hepatology 2012;55(2):455-64.
9 Tutar O, Beser ÖF, Adaletli I, Tunc N, Gulcu D, Kantarci F, et al. Shear wave elastography in the evaluation of liver fibrosis in children. Journal of pediatric gastroenterology and nutrition 2014;58(6):750-5.
10 Paparo F, Corradi F, Cevasco L, Revelli M, Marziano A, Molini L, et al. Real-time elastography in the assessment of liver fibrosis: a review of qualitative and semi-quantitative methods for elastogram analysis. Ultrasound in medicine & biology 2014;40(9):1923-33.
11 Papastergiou V, Tsochatzis E, Burroughs AK. Non-invasive assessment of liver fibrosis. Annals of Gastroenterology 2012;25(3):218.
12 Sebastiani G, Vario A, Guido M, Alberti A. Sequential algorithms combining non-invasive markers and biopsy for the assessment of liver fibrosis in chronic hepatitis B. World journal of gastroenterology 2007;13(4):525.
13 Sande JA, Verjee S, Vinayak S, Amersi F, Ghesani M. Ultrasound shear wave elastography and liver fibrosis: A Prospective Multicenter Study. World journal of hepatology 2017;9(1):38.
14 Abubakar I, Tillmann T, Banerjee A. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2015;385(9963):117-71.

15 Wang H, Naghavi M, Allen C, Barber RM, Bhutta ZA, Carter A, et al. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. The lancet 2016;388(10053):1459-544.
16 Cohn SM, Brower ST. Elective general surgery: an evidence-based approach: PMPH-USA; 2012.
17 Tsochatzis EA, Bosch J, Burroughs AK. Liver cirrhosis. The Lancet 2014;383(9930):1749-61.
18 Ibrahim AA, El Nabawy WM, Atta MI, Salem MN, Naiem M. Association between Serum Sodium Level and Severity of Complications in Liver Cirrhosis. women 2011;1:2.
19 Iredale JP. Cirrhosis: new research provides a basis for rational and targeted treatments. Bmj 2003;327(7407):143-7.
20 Puche JE, Saiman Y, Friedman SL. Hepatic stellate cells and liver fibrosis. Comprehensive Physiology 2013.
21 Moore KP, Aithal GP. Guidelines on the management of ascites in cirrhosis. Gut 2006;55(suppl 6):vi1-vi12.
22 Blei AT. Portal hypertension and its complications. Current opinion in gastroenterology 2007;23(3):275-82.
23 Garcia-Tsao G. The Use of Nonselective Beta Blockers for Treatment of Portal Hypertension. Gastroenterology & Hepatology 2017;13(10):617 Sundaram V, Shaikh OS. Hepatic encephalopathy: pathophysiology and emerging therapies. Medical Clinics of North America 2009;93(4):819-36.
26 Salerno F, Gerbes A, Ginès P, Wong F, Arroyo V. Diagnosis, prevention and treatment of hepatorenal syndrome in cirrhosis. Gut 2007 03/27;56(9):1310-8.