Original Article

Positive Predictive Value of Shear Wave Elastography in Predicting the Stage of Liver Fibrosis Taking Histopathology as Gold Standard

Rabia Asif, Amber Goraya and Abid Ali Qureshi

ABSTRACT

Objective: The objective of this study was to determine the positive predictive value of shear wave elastography (SWE) in predicting the stage 3 of liver fibrosis taking histopathology as gold standard.

Study Design: A cross-sectional study.

Place and Duration of Study: This study was conducted at the Research was conducted at Department of Diagnostic Radiology, Children Hospital Lahore, from April, 2019 to October, 2019.

Materials and Methods: This study involved 117 children of both genders aged between 1 to 15 years having chronic liver disease. Ultrasound abdomen was performed and stage 3 fibrosis was diagnosed on shear wave elastography (7.1-12.0 kPa). The diagnosis was later confirmed on histopathology of liver tissue. Diagnosis of histopathology was taken as gold standard and results of SWE on ultrasound were judged accordingly as true positive or false positive.

Results: The mean age of the children was 8.4±4.4 years while the mean weight was 32.1±14.9 Kg. There were 74 (63.2%) male and 43 (36.8%) female children. Histopathology confirmed diagnosis of Stage-3 liver fibrosis in 107 (91.5%) cases. Taking histopathological diagnosis of stage-3 liver fibrosis as gold standard, there were 107 (91.5%) true positive and 10 (8.5%) false positive cases. It yielded a positive predictive value of 91.5% for SWE on ultrasound in predicting stage 3 of liver fibrosis taking histopathology as gold standard. Similar positive predictive value was noted across various subgroups of children based on age (p-value=0.998), gender (p-value=0.824) and weight (p-value=0.969).

Conclusion: The positive predictive value of shear wave elastography on ultrasound was found to be 91.5% in predicting stage 3 hepatic fibrosis taking histopathology of liver tissue as gold standard.

Key Words: Hepatic Fibrosis, Ultrasound, Shear Wave Elastography, Positive Predictive Value

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INTRODUCTION

Liver fibrosis is considered to be a complex fibrogenic and inflammatory process resulting due to chronic liver injury and is known to represent initial steps in development of liver cirrhosis. Liver cirrhosis is an important health issue globally.[1,2]Known etiologies of liver cirrhosis vary geographically as alcoholism, chronic hepatitis C as well as nonalcoholic fatty lives disease (NAFLD) are the most frequent in developed western part of the world while chronic hepatitis B is the most common cause in Asia-Pacific Region.[3,4] Ultrasound-guided liver biopsy is considered to be the "gold standard" for diagnosing liver cirrhosis. However, ultrasonography (US), computed tomography, and magnetic resonance imaging (MRI) are being used to stage the fibrosis of the liver by non-incisive methods.[5] Guibal et al. in 2016 conducted a study on the patients suffering with liver diseases and found that the shear wave elastography (SWE) has positive predictive value (PPV) of 91.7% in predicting stage 3 fibrosis.[6]

There is no such local clinical study present on this topic to the best of our knowledge up to date. The SWE not only can lead to early detection of the fibrosis of the liver but also stages the fibrosis which corresponds with histopathology. As the PPV varies with the prevalence of disease there is a need to conduct this study in local population so that the PPV of SWE in determining the stage of fibrosis and progression of disease and this will ultimately help the clinicians to opt the management

Department of Paediatric Radiology, The Children's Hospital & Institute of Child Health, Lahore.

Correspondence: Dr. Amber Goraya, Assistant Professor, Department of Paediatric Radiology, The Children's Hospital & Institute of Child Health, Lahore.
Contact No: 03324161904
Email: amber.goraya@yahoo.com

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plane which reduces the progression of disease and to stop or delay reaching the cirrhosis and to reverse the fibrosis if the disease is treatable. The objective of this study was to determine the positive predictive value of shear wave elastography (SWE) in predicting the stage 3 of liver fibrosis taking histopathology as gold standard.

MATERIALS AND METHODS

This cross sectional study was done at Department of Diagnostic Radiology, Children Hospital Lahore, from 11/04/2019 to 10/10/2019. Approval from "Institutional Ethical Committee" was taken for this study. Informed consent was sought from parents or guardians of all study participants. A sample size of 117 cases was calculated by 95% confidence level and 5% margin of error while taking expected PPV of SWE as 91.7%.[6]

Inclusion criteria was patients of both sex groups with ages in the range of 1-15 years having stage-3 liver fibrosis on SWE. Patients with abnormal liver enzymes (ALT or AST >40IU) for more than 8 weeks as per clinical record undergoing SWE in the range of 7.1-12.0 kPa were labeled to have stage-3 fibrosis. All patients who had Hepatitis B or C on ELISA were excluded. Patients with congenital heart defects were also excluded. Patients who had abnormal peripheral smear as per clinical record were also not included. Patients with bleeding disorder (INR >1.5), ascites on ultrasound and histologically proven liver malignancy as per clinical record were also not included in this study.

After approval from ethical review committee of the hospital, 117 patients who presented in the radiology department, Children Hospital, Lahore fulfilling inclusion and exclusion criteria were enrolled. SWE was performed in the segment 5 of the liver. The right arm was placed in maximum abduction to enlarge the space between the ribs. During SWE acquisition, the patient was asked to stop breathing for 5 seconds. Real-time SWE 2D color map of the stiffness (in kPa) was frozen after a stabilization of at least 3 seconds. Under aseptic measures using 16-gauge needle, liver biopsy was taken and sent for the histopathology examination as per hospital protocol. Stage-3 fibrosis on histopathology was labeled as microscopic examination of liver showing bridging fibrosis along with architectural distortion.

All the data and information were noted into a specially made proforma. All the SWE were performed on the same machine by the same consultant of the radiology department and all the histopathologies were reported by the same consultant of the histopathology department to eliminate bias.

All the collected data was entered and analyzed through SPSS version 26.0. Numerical variables like age and body weight were presented by mean ±SD. Categorical variables like gender and histological diagnosis of stage 3 fibrosis were shown as frequency and percentage. Positive predictive value has been calculated by the following formula and is presented as frequency and percentage.

$$PPV = \frac{\text{True positive}}{\text{True positive + False positive}} \times 100$$

True Positive cases were patients having stage-3 liver fibrosis on SWE later found to be true on histopathology. False Positive cases were patients having stage-3 liver fibrosis on SWE later found to be false on histopathology. Data was stratified for age, gender and weight to address effect modifiers. Post-stratification, chi-square test was applied taking p-value≤0.05 as significant.

RESULTS

The age of the children ranged from 1 year to 15 years with a mean of 8.4±4.4 years. There were 74 (63.2%) male and 43 (36.8%) female children with a male to female ratio of 1.7:1. The weight of these children ranged from 8 Kg to 55 Kg with a mean of 32.1±14.9 Kg as shown in Table 1.

Table No.1: Demographic Characteristics of Cases

Characteristics		Number (%)
Age (years)	<5	35 (29.9%)
	5-10	36 (30.8%)
	>10	46 (39.3%)
Gender	Male	74 (63.2%)
	Female	43 (36.8%)
Weight (kg)	≤23	44 (37.6%)
	24-39	27 (23.1%)
	≥40	46 (39.3%)

Table No.2: Detail of PPV across various subgroups of children

Characteristics		Cases Outcome		PPV	P-value
		True Positive (n=107)	False Positive (n=10)		
Age (years)	<5	32 (91.4%)	3 (8.6%)	91.4%	0.998
	5-10	33 (91.7%)	3 (8.3%)	91.7%	
	>10	42 (91.3%)	4 (8.7%)	91.3%	
Gender	Male	68 (91.9%)	6 (8.1%)	91.9%	0.824
	Female	39 (90.7%)	4 (9.3%)	90.7%)	
Weight (kg)	≤23	40 (90.0%)	4 (9.1%)	90.9%	0.969
	24-39	25 (92.6%)	2 (7.4%)	92.6%)	
	≥40	42 (91.3%)	4 (8.7%)	91.3%	

Histopathology confirmed diagnosis of stage-3 liver fibrosis in 107 (91.5%) cases as shown in Table 2. Taking histopathological diagnosis of stage-3 liver fibrosis as gold standard, there were 107 (91.5%) true positive and 10 (8.5%) false positive cases. It yielded a positive predictive value of 91.5% for SWE on ultrasound in predicting stage 3 of liver fibrosis taking histopathology as gold standard.

Similar PPV was noted across various subgroups of children based on age (p-value=0.998), gender (p-value=0.824) and weight (p-value=0.969) as shown in Tables 2.

DISCUSSION

Recent studies have reported high positive predictive value of SWE in the non-invasive diagnosis of sage 3 fibrosis among such patients,[7-9] however, there was no such local published study which made us plan this work.

In the present study, the mean age of the children was 8.4±4.4 years. Parkash et al reported similar mean age of 8.5±2.7 years among children presenting with liver fibrosis.[10] A similar mean age of 6.9±1.8 years has been reported by Hashmi et al among such children presenting at Shifa International Hospital, Islamabad[11] while Tahir et al observed it to be 6.4±4.3 years at Fauji Foundation Hospital Rawalpindi.[12] A comparable mean age of 10.7±2.1 years was found by Dhole et al from India.[13]

We noted male to female ratio of 1.7:1. Similarly, male predominance has been reported in a number of local studies where Hashmi et al observed it to be 2.2:1 at Shifa International Hospital, Islamabad[11] and Anwar et al. reported it to be 2.1:1.[14] Dhole et al found male predominance from India in such children with male to female ratio of 1.5:1[13] while Rukunuzzaman et al observed it to be 1.4:1 in Bangladesh.[15]

We found that SWE had positive predictive value of 91.5% in predicting stage 3 of liver fibrosis taking histopathology as gold standard. Our results are in line with those of Ferraioli et al who reported similar PPV of 91.3% for shear wave elastography in Italy[16] and Guibal et al who reported it to be 91.7% in France.[6] Thiele et al reported it to be 90.0% in Denmark.[7] Comparable positive predictive value of 95.7% has been reported by Zeng et al in China.[8] Cassinotto et al observed much lower positive predictive value of 52.6% in a French study[9] while Jeong et al[17] and Zhuang et al[18] reported much higher PPV of 97.7% and 98.4% in South Korea and China respectively.

One of the limitations of this research was that we didnot consider the effect of this timely staging of liver fibrosis and anticipated management on the outcome of such children which would have further highlighted the role of SWE in the management planning of such cases.

CONCLUSION

The positive predictive value of shear wave elastography on ultrasound was found to be 91.5% in predicting stage 3 hepatic fibrosis taking histopathology of liver tissue as gold standard regardless of patient's age, gender and weight which along with its non-invasive and radiation free nature and widespread and bedside availability advocate its preferred use in future practice so that risk stratification and anticipated management may improve the outcome of such children.

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Author's Contribution:

Concept & Design of Study:	Rabia Asif
Drafting:	Amber Goraya
Data Analysis:	Abid Ali Qureshi
Revisiting Critically:	Rabia Asif, Amber Goraya
Final Approval of version:	Rabia Asif

Conflict of Interest: The study has no conflict of interest to declare by any author.

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