Original article

Comparison of Two-Dimensional Shear Wave Elastography Versus Fibrosis-4 Index for Evaluation of Liver Fibrosis in Chronic Hepatitis B Patients

Umer Farooq[1], Rimsha Shams[1,*], Humaira Riaz[1], Madiha Azam[1], Ghanwa[1], Ayesha[1], Zulaikha[1]

Abstract

Introduction: In countries like Pakistan, chronic hepatitis B infection is a major public health issue. Accurate assessment of liver fibrosis is crucial for proper medical care. Promising techniques include 2D-SWE and serum-based models like FIB-4. CHB infection contribute to liver fibrosis, cirrhosis, and liver cancer. Accurate assessment of liver fibrosis is crucial for proper care, using non-invasive techniques like 2D-SWE and serum-based fibrosis models like FIB-4.
Objective: To evaluate liver fibrosis among patients with CHB infection, we aim to compare the diagnostic performance of 2D-SWE and FIB-4.
Study Design: This research was a Quasi Experimental study.
Patients and Methods: The study involved a sample of 100 individuals with chronic Hepatitis B infection, selected using a sequential non-probability sampling technique. Eligibility for the study requires patients to demonstrate laboratory indications of chronic hepatitis B infection and provide either hepatic biopsy or fibro-scan results. Exclusion criteria involved patients with congestive cardiac failure, hepatic focal lesions, portal vein thrombosis, history of hepatic interventional procedures, or fibrosis due to other causes. Written informed consent was obtained from participants. The process involved in data collection included; performing 2D-SWE and calculating fibrosis-4 scores using age, platelet count, and serum liver enzyme levels. This information was then documented on a specific proforma.
Results: The research comprised of a sample of 100 patients diagnosed with chronic hepatitis B, yielding diverse findings. The analysis of gender distribution indicated the presence of 67 male and 33 female participants. Descriptive statistics were provided for several variables, encompassing age (with a mean of 37.46, ranging from 30 to 49 years), alanine aminotransferase (ALT) level (with a mean of 76.10, ranging from 25 to 312 IU/L), and aspartate aminotransferase (AST) level (with a mean of 136.98, ranging from 55 to 456 IU/L), platelet count (ranging from 70 to 200 with a mean of 114.43), Fibrosis 4 Index score (ranging from 0.93 to 7.83 with a mean of 2.28), and duration of disease (ranging from 1 to 10 years with a mean of 3.93). The crosstabulation table showed the distribution of Ishak levels based on elastography results. The statistical analysis revealed significant differences in Fibrosis-4 Index across different elastography groups. Post hoc analyses further supported these findings, indicating significant mean differences between specific elastography groups. These results emphasize the importance of elastography in assessing liver fibrosis in chronic hepatitis B patients.
Conclusion: Evaluating liver fibrosis in chronic hepatitis B patients can be done effectively using non-invasive methods like 2D-SWE and FIB-4. However, Standardized protocols and guidelines are needed to integrate non-invasive techniques like 2D-SWE and FIB-4 into clinical care for chronic hepatitis B patients.

Keywords: 2 D Elastography, Fibrosis 4 Index, Chronic Hepatitis B infection

[1] Radiology Department, Benazir Bhutto Hospital, Rawalpindi
*** Corresponding author**: Rimsha Shams (rimshashams42@gmail.com)
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1. Introduction

Hepatitis B virus (HBV) infection is a significant public health issue, especially in developing countries like Pakistan, where about 15% of infected individuals develop chronic hepatitis B (CHB), leading to serious liver complications1. Accurate assessment of liver fibrosis is essential for managing CHB. While liver biopsy is the gold standard, its invasiveness limits its use 2D shear wave elastography (2D-SWE) has emerged as a valuable non-invasive alternative, with a sensitivity of 88% and specificity of 83%.[2]

It is recommended for liver stiffness measurements but requires skilled radiologists3. Additionally, serum fibrosis models like the FIB-4 index, which has high specificity (96%) but lower sensitivity (42%), offer further non-invasive assessment options[4]. A comparative study of the FIB-4 indexes and 2D-SWE is needed to evaluate their diagnostic performance in assessing liver fibrosis in CHB patients, aiding healthcare providers in optimizing patient management.

2. Materials & Methods

It was a Qausi Experimental study conduded in Department of Radiology Benazir Bhutto Hospital, Rawalpindi. The study was conducted from 2nd May 2021 to 2nd October 2021. A total of 100 patients have been calculated using the WHO sample size calculator.

Keeping the confidence interval 95% and margin of error 10%. Non-probability consecutive sampling. Inclusion Criteria: All patients, males and females with chronic hepatitis B infection with proven laboratory evidence on PCR.

All patients with the results of fibrosis index or positive report of hepatic enzymes and raised platelet count. Available hepatic biopsy is appreciated but fibro-scan available results will also be considered.

Exclusion Criteria: Patients with congestive heart failure. Patients with a hepatic focal lesion (benign or malignant). Patients with portal vein thrombosis. Patients have a history of hepatic interventional procedure (ERCP, PTC radiofrequency ablation, or chemoembolization). Patients have fibrosis due to reasons other than CHB infection (primary biliary cirrhosis, primary sclerosing cholangitis, or autoimmune hepatitis).

The data collection procedure was presented in front of the ethical review board of the Rawalpindi Medical University, and it was started after approval from ERB. All patients meeting inclusion criteria were inducted into this study. A total of 100 patients were selected as per sample size.

Written informed consent was taken for participation in the study. A consecutive sampling technique was employed to select patients for the study. This sampling technique was used to minimize selection bias. All patients underwent 2D-SWE and fibrosis-4 score the patients was calculated using their age, platelet count, and serum liver enzymes levels. All the information was recorded under the supervision of a Consultant Radiologist on a proforma attached to this synopsis.

SPSS version 25 is used to collect and analyze data. Gender, as a qualitative variable, was presented in terms of frequency and percentages. Mean ± Standard deviation was used to assess continuous variables, such as age, duration of symptoms, time since hepatitis B diagnosis, ALT levels, AST levels, and platelet count. To compare 2D elastography and Ishak fibrosis levels, the Chi-square test was utilized, while a one-way ANOVA was employed to compare the fibrosis-4 index with 2-D elastography results. A significance level of $p \leq 0.05$ was considered for statistical significance.

3. Results

There are 67 male and 33 female chronic hepatitis B patients in this study. The minimum value of age was 30 years, and the maximum value of age was 49 years. The average age of the respondents was 37.46±5.283 years. The minimum value of ALT was 25 and the maximum value of ALT was 312. Minimum & maximum AST: The minimum value of AST was 55 and the maximum AST value was 456. The mean ALT of the patients was 136.98±74.48IU/L. The minimum platelet count was 70 and the maximum platelet count was 200. The mean platelet count of the patients was 114.43±27.92IU/L. The minimum Fibrosis 4 Index score was 0.93 and the maximum Fibrosis 4 Index score was 7.83.The mean Fibrosis 4 Index score of the patients was 2.28±1.73.The minimum duration of diseasee was 1 year, and the maximum duration of disease was 10 years. The mean duration of disease of the patients was 3.93±2.081.

The p-value associated with the chi-square statistic is 0.000, indicating that the association between "Elastography" and "Ishak level" is statistically significant at a significance level of .05. The analysis revealed a significant main effect of group on Fibrosis 4 index ($F(3, 96) = 82.477$, $p < .001$). The between-groups analysis indicated a significant difference in mean Fibrosis-4 index among the groups (M = 70.897). Additionally, the within-groups analysis revealed a smaller mean square value (M = .860) compared to the between-groups mean square, suggesting less variation within the groups. These findings suggest that the group variable significantly influences the Fibrosis-4 index, indicating a clear distinction in Fibrosis severity across the different groups. While comparing F3-F4 to F0, F0-F1, and F2-F3, all comparisons revealed significant mean differences.

Table 3 revealed significant differences in mean fibrosis-4 index among the Elastography groups. Comparing Elastography group F0 to F0-F1, there was a non-significant mean difference of -0.38079 (SE = 0.25458, p = 0.444), with a confidence interval ranging from -1.0464 to 0.2848. Comparisons between F0 and F2-F3, as well as F0 and F3-F4, yielded significant mean differences of -1.40490 (SE = 0.26379, $p < 0.001$) and -4.67678 (SE = 0.32719, $p < 0.001$), respectively.

The confidence intervals for these comparisons were -2.0946 to -0.7152 and -5.5323 to -3.8213, respectively.

Similarly, when comparing F0-F1 to F0, F2-F3, and F3-F4, significant mean differences were observed. The mean differences were 0.38079 (SE = 0.25458, p = 0.444) for F0-F1 vs. F0, -1.02411 (SE = 0.22920, p < 0.001) for F0-F1 vs. F2-F3, and -4.29598 (SE = 0.30000, p < 0.001) for F0-F1 vs. F3-F4.

The corresponding confidence intervals were -0.2848 to 1.0464, -1.6234 to -0.4249, and -5.0804 to -3.5116, respectively. For the comparison between F2-F3 and F0, F0-F1, and F3-F4, significant mean differences were observed. The mean differences were 1.40490 (SE = 0.26379, p < 0.001) for F2-F3 vs. F0, 1.02411 (SE = 0.22920, p < 0.001) for F2-F3 vs. F0-F1, and -3.27187 (SE = 0.30786, p < 0.001) for F2-F3 vs. F3-F4. The corresponding confidence intervals were 0.7152 to 2.0946, 0.4249 to 1.6234, and -4.0768 to -2.4669, respectively. Lastly, when comparing F3-F4 to F0, F0-F1, and F2-F3, all comparisons revealed significant mean differences.

The mean differences were 4.67678 (SE = 0.32719, p < 0.001) for F3-F4 vs. F0, 4.29598 (SE = 0.30000, p < 0.001) for F3-F4 vs. F0-F1, and 3.27187 (SE = 0.30786, p < 0.001) for F3-F4 vs. F2-F3. The corresponding confidence intervals were 3.8213 to 5.5323, 3.5116 to 5.0804, and 2.4669 to 4.0768, respectively.

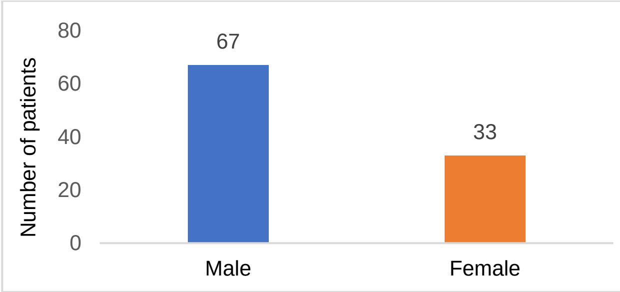

Fig 1: Gender Distribution in Patients

Table 1: Descriptive statistics of all continuous variables

	Min	**Max**	**Mean± SD**
Age (Years)	30	49	37.46±5.28
ALT levels (IU/L)	25	312	76.10±61.08
AST levels (IU/L)	55	456	136.98±74.48
Platelets count (10^3dl/L)	70	200	114.43±27.92
Fibrosis- 4 Index Score	0.93	7.83	2.28±1.73
Duration of Disease (years)	1	10	3.93±2.09

Table 2: Post Hoc Analysis of Fibrosis Scores based on Elastography Groups using the Least Significant Difference (LSD)

(I) Elastography	**(J) Elastography**	**Mean Difference (I-J)**	**Std. Error**	**Sig.**	**95% Confidence Interval**	
					Lower Bound	**Upper Bound**
F0	F0-F1	-.38079	.25458	.138	-.8861	.1245
	F2-F3	-1.40490*	.26379	.000	-1.9285	-.8813
	F3-F4	-4.67678*	.32719	.000	-5.3263	-4.0273
F0-F1	F0	.38079	.25458	.138	-.1245	.8861
	F2-F3	-1.02411*	.22920	.000	-1.4791	-.5692
	F3-F4	-4.29598*	.30000	.000	-4.8915	-3.7005
F2-F3	F0	1.40490*	.26379	.000	.8813	1.9285
	F0-F1	1.02411*	.22920	.000	.5692	1.4791
	F3-F4	-3.27187*	.30786	.000	-3.8830	-2.6608
F3-F4	F0	4.67678*	.32719	.000	4.0273	5.3263
	F0-F1	4.29598*	.30000	.000	3.7005	4.8915
	F2-F3	3.27187*	.30786	.000	2.6608	3.8830

*. The mean difference is significant at the 0.05 level.

Table 3: Post Hoc Analysis of Multiple Comparisons of Fibrosis Scores based on Elastography Groups (Tukey HSD)

(I) Elastography	(J) Elastography	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
F0	F0-F1	-.38079	.25458	.444	-1.0464	.2848
	F2-F3	-1.40490*	.26379	.000	-2.0946	-.7152
	F3-F4	-4.67678*	.32719	.000	-5.5323	-3.8213
F0-F1	F0	.38079	.25458	.444	-.2848	1.0464
	F2-F3	-1.02411*	.22920	.000	-1.6234	-.4249
	F3-F4	-4.29598*	.30000	.000	-5.0804	-3.5116
F2-F3	F0	1.40490*	.26379	.000	.7152	2.0946
	F0-F1	1.02411*	.22920	.000	.4249	1.6234
	F3-F4	-3.27187*	.30786	.000	-4.0768	-2.4669
F3-F4	F0	4.67678*	.32719	.000	3.8213	5.5323
	F0-F1	4.29598*	.30000	.000	3.5116	5.0804
	F2-F3	3.27187*	.30786	.000	2.4669	4.0768
*. The mean difference is significant at the 0.05 level.						

4. Discussion

This research evaluated the diagnostic accuracy of 2D shear-wave elastography (2D-SWE) and the Fibrosis 4 Index in chronic hepatitis B (CHB) patients. The study found a significant correlation between 2D-SWE findings and Ishak fibrosis grading, highlighting elastography's value in assessing liver fibrosis5. AUROCs were 0.906 for significant fibrosis and 0.955 for cirrhosis, with a meta-analysis showing an AUROC of 0.92 for significant fibrosis, reinforcing 2D-SWE's reliability. Comparative studies revealed that 2D-SWE outperformed serum fibrosis models, with AUROCs of 0.851 versus lower values for models like APRI (0.738). Huang et al. reported even higher AUROCs for 2D-SWE in CHB patients: 0.97 for significant fibrosis and 0.98 for cirrhosis6. Variability in serum models' diagnostic capabilities was noted, with AUROCs ranging from below 0.6 to above 0.97. The Fibrosis 4 index and Forns index performed best among these models, though excluding patients with elevated ALT and AST may have impacted accuracy8. Research on 2D-SWE in Pakistan and South Asia is limited9. Studies showed AUROCs of 0.835 and 0.881 for significant fibrosis and cirrhosis, respectively, with higher values in another study (0.914 for significant fibrosis and 0.948 for cirrhosis)10. Optimal cut-off values were identified as 6.95 to 7.90 kPa for significant fibrosis and 10.1 to 11.8 kPa for cirrhosis11. The study found platelet count and ALP independently correlated with 2D-SWE values, while no correlation with ALT was observed, possibly due to population differences12. Limitations include a small sample size, focusing only on significant fibrosis and cirrhosis, and not assessing inflammation stages13. Further research is needed to establish precise cut-off values and confirm 2D-SWE's diagnostic efficacy for liver fibrosis in HCC and CHB patients, as well as its potential in guiding antiviral therapy and predicting postoperative outcomes.

5. Conclusion

In the assessment of liver fibrosis in chronic hepatitis B patients, both 2D-SWE and FIB-4 prove effective as noninvasive methods. Comparatively, previous studies have examined non-invasive techniques for evaluating liver fibrosis. Utilizing 2D-SWE and FIB-4, clinicians can acquire valuable information regarding the severity of fibrosis without the necessity of invasive liver biopsies. To integrate these noninvasive approaches into routine clinical practice for individuals afflicted with chronic hepatitis B infection, additional research and validation are required. As a result, the management of chronic hepatitis B will benefit from the development and implementation of these noninvasive methods, leading to improved patient care and outcomes.

References

1. 1. Areeba Ahsan, Muhammad Daoud Tariq, Mubashir Zafar, Hafiz Muhammad Hamza, Fatima Kaleem, Muhammad Muiz Malik, et al. Analysis of Hematological Profiles in Hepatitis B Patients; Understanding the Interplay Between Viral Infections and Blood Parameters | Opast Publishing Group [Internet]. [cited 2024 Oct 30]. Available from:

https://www.opastpublishers.com/peer-review/analysis-of-hematological-profiles-in-hepatitis-b-patients-understanding-the-interplay-between-viral-infections-and-bloo-7415.html

2. 2. Lai JCT, Liang LY, Lai-Hung Wong G. Noninvasive tests for liver fibrosis in 2024: are there different scales for different diseases? Gastroenterol Rep (Oxf) [Internet]. 2023 Dec 22 [cited 2024 Oct 30];12. Available from: https://dx.doi.org/10.1093/gastro/goae024
3. 3. Boursier J, Decraecker M, Bourlière M, Bureau C, Ganne-Carrié N, de Lédinghen V. Quality criteria for the measurement of liver stiffness. Clin Res Hepatol Gastroenterol. 2022 Jan 1;46(1):101761.
4. 4. Loomba R, Adams LA. Advances in non-invasive assessment of hepatic fibrosis. Gut [Internet]. 2020 Jul 1 [cited 2024 Oct 30];69(7):1343–52. Available from: https://gut.bmj.com/content/69/7/1343
5. 5. Seyrek S, Ayyildiz H, Bulakci M, Salmaslioglu A, Seyrek F, Gultekin B, et al. Comparison of Fibroscan, Shear Wave Elastography, and Shear Wave Dispersion Measurements in Evaluating Fibrosis and Necroinflammation in Patients Who Underwent Liver Biopsy. Ultrasound Q [Internet]. 2024 Mar 17 [cited 2024 Oct 30];40(1):74–81. Available from: https://journals.lww.com/ultrasound-quarterly/fulltext/2024/03000/comparison_of_fibroscan,_shear_wave_elastography,.11.aspx
6. 6. Huang Z, Zheng W, Zhang YJ, Xu L, Chen J Bin, Chen JC, et al. Assessing Hepatic Fibrosis Using 2-D Shear Wave Elastography in Patients with Liver Tumors: A Prospective Single-Center Study. Ultrasound Med Biol [Internet]. 2017 Nov 1 [cited 2024 Oct 30];43(11):2522–9. Available from: https://pubmed.ncbi.nlm.nih.gov/28807448/
7. 7. Garg M, Karpinski M, Matelska D, Middleton L, Burren OS, Hu F, et al. Disease prediction with multi-omics and biomarkers empowers case–control genetic discoveries in the UK Biobank. Nature Genetics 2024 56:9 [Internet]. 2024 Sep 11 [cited 2024 Oct 30];56(9):1821–31. Available from: https://www.nature.com/articles/s41588-024-01898-1
8. 8. Ballestri S, Mantovani A, Baldelli E, Lugari S, Maurantonio M, Nascimbeni F, et al. Liver Fibrosis Biomarkers Accurately Exclude Advanced Fibrosis and Are Associated with Higher Cardiovascular Risk Scores in Patients with NAFLD or Viral Chronic Liver Disease. Diagnostics 2021, Vol 11, Page 98 [Internet]. 2021 Jan 9 [cited 2024 Oct 30];11(1):98. Available from: https://www.mdpi.com/2075-4418/11/1/98/htm
9. 9. Ng KH, Wong JHD, Leong SS. Shear wave elastography in chronic kidney disease – the physics and clinical application. Phys Eng Sci Med [Internet]. 2024 Mar 1 [cited 2024 Oct 30];47(1):17–29. Available from: https://link.springer.com/article/10.1007/s13246-023-01358-w
10. 10. Jia X, Song E, Liu Y, Chen J, Wan P, Hu Y, et al. Identification and multicentric validation of soluble CDCP1 as a robust serological biomarker for risk stratification of NASH in obese Chinese. Cell Rep Med [Internet]. 2023 Nov 21 [cited 2024 Oct 30];4(11). Available from: http://www.cell.com/article/S2666379123004342/fulltext
11. 11. Chen S, Jiang T. Preoperative noninvasive assessment for liver fibrosis in hepatocellular carcinoma patients with chronic hepatitis B: Comparison of two-dimensional shear-wave elastography with serum liver fibrosis models. Eur J Radiol. 2020 Dec 1;133:109386.
12. 12. Huang Z, Zhou J, Lu X, Zhang T, Xu S, Jin J, et al. How does liver steatosis affect diagnostic performance of 2D-SWE.SSI: assessment from aspects of steatosis degree and pathological types. Eur Radiol [Internet]. 2021 May 1 [cited 2024 Oct 30];31(5):3207–15. Available from: https://link.springer.com/article/10.1007/s00330-020-07288-5
13. 13. Venkatesh SK, Torbenson MS. Liver fibrosis quantification. Abdominal Radiology 2022 47:3 [Internet]. 2022 Jan 12 [cited 2024 Oct 30];47(3):1032–52. Available from: https://link.springer.com/article/10.1007/s00261-021-03396-y