

ORIGINAL ARTICLE

ASSOCIATION OF FIBROTIC CHANGES IN LIVER ON FIBRO-SCAN WITH VIRAL LOAD AND DURATION OF HEPATITIS C INFECTION -A PILOT STUDY

Muhammad Arshad¹, Iqra Manzoor², Khalid Hussain Memon², Asif Haider², Umer Aziz Khan³, Iraj Nayab⁴, Zareen Fatima²

¹The Institute of Nuclear Medicine, Oncology and Radiotherapy, Abbottabad, ²University Institute of Radiological Sciences and Medical Imaging Technology, Lahore, ³NIMS Teaching Hospital, Abbottabad, ⁴Hazara University, Mansehra-Pakistan

Background: Hepatitis C is a diverse illness that causes significant death and morbidity. The hepatitis C virus infects hundreds of millions of individuals globally (HCV). More than 80% of those infected develop chronic infection; the remaining 10–20% recovers spontaneously through natural immunity. Acute hepatitis is only icteric in 20% of individuals and is seldom severe. **Methods:** A pilot study was conducted at INOR hospital Abbottabad. Eleven hepatitis C positive and 10 hepatitis C negative participants were included in the study. **Results:** A significant difference correlation was found between viral load and SWE quantification for fibrosis stage in Kilo-Pascal, $r=0.904$ (p -value=0.000 $<a=0.05$). HCV positive patients showed a viral load of (Mean \pm SD) 128,185.8 \pm 153,719.1. **Conclusion:** Although a biopsy is considered to be gold standard for determining the degree of damage caused by chronic viral hepatitis, it is far from perfect. Liver elastography is intriguing techniques that can help physicians make difficult decisions while treating viral hepatitis. This study showed that fibrotic changes of liver are directly proportional to the presence of viral load in blood. The greater the viral load more severe fibrosis will be seen. Age also plays a role in severity of fibrosis, however, more studies on larger population is required to support this statement.

Keywords: Cirrhosis; Fibroscan; Hepatic events; Liver stiffness measurement Fibrosis; Elastography; Metavir score; Viral load

Citation: Arshad M, Manzoor I, Memon KH, Haider A, Khan UA, Nayab I, *et al.* Association of fibrotic changes in liver on fibro-scan with viral load and duration of hepatitis C infection -A pilot study. J Ayub Med Coll Abbottabad 2023;35(1):110–3.

DOI: 10.55519/JAMC-01-11171

INTRODUCTION

Hepatitis is a Greek term that combines the words "hepa" and "itis" meaning inflammation of liver. Hepatitis C is one of the leading causes of mortality for millions of people globally. It is one of the primary causes of liver cirrhosis and carcinomas, both of which are fatal.¹ A report stated that over 700,000 individuals died of disorders related to Hepatitis C, making it more common than cancer and cirrhosis, which kill 167,000 and 326,000 people, respectively.² Virus causes hepatitis C, which results in long-term illness. Blood contact, transfusions, vertical transmission, needle stick injuries, sexual contact, and intravenous drug usage are the most prevalent ways it spreads.³

Hepatitis C produces liver inflammation, which causes discomfort on the right side of abdomen, and leads to enlargement of liver. As a result of the prolonged inflammation and infection, lymphocyte cells enter the portal system, and liver cells die.⁴ The liver's cell and tissue become inflamed, and the liver needs to replace them quickly. Some develop scarring and fibrosis, while others

experience hepatocyte frenzy and malignant replication of cells, ending in hepatocellular carcinoma.⁵

Although antiviral therapy with nucleotide analogues (NUCs) substantially lowers HBV, liver-related diseases such as decompensation of the liver, HCC, and deaths caused by liver disorders continue to occur and represent a key watershed in the CHB patient care strategy.⁶ Because LREs are more common in people with severe liver scarring and cirrhosis, early detection of advanced stage fibrosis and cirrhosis, as well as severity evaluation, are crucial for developing suitable surveillance and therapy strategies. Although biopsy of the liver was once regarded as the gold standard for assessing liver fibrosis⁷, it is vulnerable to sampling error and interpretation ambiguity⁸. Recently, an accurate, reliable, and dependable liver stiffness measurement (LSM) using transient elastography (FibroScan®) for evaluating liver fibrosis has been created.^{9,10} Furthermore, because LSM may be expressed quantitatively as a continuous variable, clinicians can grade the level of liver fibrosis in cirrhotic patients

and predict the likelihood of acquiring liver-related comorbidities and HCC.¹¹⁻¹³

A study stated that if the FibroScan score was >9.6 kPa, it was feasible to properly determine if an individual had stage 3 or higher fibrosis (advanced fibrosis). Based on the American Association for the Study of Liver Diseases (AASLD) practice recommendations for the management of hepatitis C virus (HCV) infection, patients with stage 3 or greater fibrosis are an essential category to treat since they have the most immediate need for medication. Because FibroScan can accurately detect people with advanced fibrosis, it might be used to categorize patients based on the severity of their treatment needs.¹⁴

Fibro scan is a straightforward, non-invasive examination that takes around 5 minutes to complete. It is use to assess liver stiffness in different liver illnesses since it is not affected by the aetiology of the disease. Fibro Scan is a painless imaging procedure that evaluates scarring, or fibrosis, produced by numerous liver illnesses. It is a safer, non-surgical alternative to liver biopsy. Fibro Scan creates a picture of the liver by detecting the speed of sound waves traveling through it, comparable to ultrasound. The colour hues in that picture then allow radiologists to evaluate the extent and location of scarring within a patient's liver.

MATERIAL AND METHODS

A one-month pilot research was carried out at INOR Hospital Abbottabad. Case group inclusion criteria were all genders, all ages, and HCV positive patients. Both genders, all ages, and individuals with negative HCV were included in the Control group. Patients that were uncooperative were eliminated from the study.

Following the receipt of written informed permission from subjects. All subjects were examined to ultrasonography with Aplio-500 2.5 MHz vs. 3.5 MHz for the M probe. The participants were laid supine, and gel was applied to the probe. With the patient laying supine, the ultrasonic probe was pushed against the skin (intercostal region) above the liver. The probe produces a vibration and then measures the velocity of the resulting shear wave as it travels through the liver, yielding ten successful readings. The system then computed the median and interquartile range of all successful measurements (in kilopascals, kPa).

RESULTS

Total 21 patients were included in this pilot study which was further divided in 2 groups. Group “A” enrolled 11 HCV positive patients. Group “B” included 10 HCV negative participants. Mean±SD

age was measured at 95% confidence level. Age of group A was 37.4±7.3 years and group B was 47.7±9.2 years. Out of 21 participants 6 (28.5%) were females and 15 (71.4%) were males. out of 22 participants 9 had metavir score of F0, 4 participants had metavir score of F1, 2 had F2, 5 had F3 and 1 participant had metavir score of F4. Out of 21 participants 10 patients were normal 11 had different degrees of fibrosis and scarring.

Table-1: Frequency distribution

Variables	Frequency	Percentage	
Gender	Male	15	71.4
	Female	6	28.5
Metavir Score	F0	9	42.8
	F1	4	19.0
	F2	2	9.5
	F3	5	23.8
	F4	1	4.7
Fibrosis	Normal	10	47.6
	Normal To Mild	4	19.0
	Mild To Moderate	2	9.5
	Moderate To Severe	4	19.0
Degree of Scarring	Severe	1	4.7
	Normal	9	42.8
	Fibrosis with septa	2	9.5
	Fibrosis without septa	4	19.0
	Septa without cirrhosis	5	23.8
	1	4.7	

A significant difference correlation was found between viral load and SWE quantification for fibrosis stage in Kilo-Pascal, $r= 0.904$ (p -value=0.000 $<a=0.05$). HCV positive patients showed a viral load of (Mean±SD) 128,185.8 ±153,719.1.

DISCUSSION

FibroScan is a non-invasive diagnostic that assesses liver elasticity, which has been associated to fibrosis. Chronic hepatitis C virus (HCV) infection is still a leading cause of liver-related mortality worldwide, accounting for approximately 25% of HCC and 25% of liver cirrhosis.¹⁴ This virus infects around 3 percent of the total global population. It is more prevalent in underdeveloped and developing continents, such as Africa (13%), with Egypt being the endemic nation (>15%).¹⁵ 10 million Pakistani population is known to be infected by hepatitis C virus. Its chronic form has been linked to hepatic cirrhosis.^{16,17} It is an epidemiological illness due to the involvement of several risk factors.^{18,19} HCV is prevalent in around 10 million persons in Pakistan.²⁰ Its frequency is not consistent throughout Pakistan but rather varies by location and community.²¹

The goal of this research is to determine the dependability of non-invasive methods for predicting the degree of hepatic fibrosis. This study found that older ages were linked to more severe liver fibrosis. This

was similar with the findings of a previous study, which discovered a relationship between the rate of fibrotic progression and an older age of infection beginning, regardless of infection duration.^{22,23} An increased viral load is directly related to stiffness level, according to this study. Another study discovered that liver rigidity and liver enzyme levels were substantially greater in individuals with advanced fibrosis, although a lower platelet count was related to advanced fibrosis.²² These measures were used to determine liver stiffness, they were much higher in those with advanced fibrosis and cirrhosis, according to earlier research.^{24,25}

Several studies on the benefits of fibroscan have been undertaken over the last decade, and a number of publications on the utility of elastography measurement in the assessment of fibrosis in chronic hepatitis have been published in France.²⁶⁻³¹ A large number of publications have been published in various nations.³²⁻³⁹ making this approach a globally known test.⁴⁰ A study from 2008⁴⁰ showed that elastography had high diagnostic accuracy for cirrhosis diagnosis. However, there was a large difference in the AUROC for the identification of severe fibrosis, which was based on the underlying liver condition. Although fibroscan is quite reliable for evaluating the degree of liver fibrosis, it cannot be used in place of a biopsy. The huge majority of trials comparing elastography and biopsy were conducted in individuals with HCV chronic hepatitis.^{31,34,38,41,42}

Seo *et al.* conducted a Korean trial in which participants with hepatitis B and C had biopsy and elastography in the same session. LS values were shown to be more closely related to scarring score in individuals with hepatitis C than in hepatitis B. Specificity and sensitivity were increased in people with chronic HCV hepatitis. The study revealed that LS assessment was more effective than HBV hepatitis for measuring liver fibrosis in patients with persistent HCV hepatitis.⁴³

CONCLUSION

Although a biopsy of the liver is the current gold standard for determining the degree of liver damage in chronic viral hepatitis, it is far from perfect. Liver elastography is intriguing techniques that can help physicians make difficult decisions while treating hepatitis. It is amazingly accurate, especially at the extremes of liver damage, is thoroughly verified and operates within its known limits. It is not a replacement for biopsy, but it can eliminate those who do not require biopsy. This study showed that fibrotic changes of liver are directly proportional to the presence of viral load in blood. Greater the viral load more severe fibrosis will be seen. Age also plays a role in severity of fibrosis, however, more studies on

larger population is required to support this statement.

AUTHORS' CONTRIBUTION

MA: The study was carried out as research work for MS degree. The primary author conducted the whole study and prepared this article. IM: She supervised the whole research work from topic selection till the completion of research& this article. KHM: The second supervisor of study. His contribution is taking approval from the administration of the institution from which the data is collected. He also helped in data analysis. AH: He helped to design data collection from the questionnaire. UAK: Help me in the statistical analysis of the collected data. IN: She also helps me in the data collection process. ZF: Help in the data analysis.

REFERENCES

1. Zhang HC, Zhu T, Hu RF, Wu L. Contrast-enhanced ultrasound imaging features and clinical characteristics of combined hepatocellular cholangiocarcinoma: comparison with hepatocellular carcinoma and cholangiocarcinoma. *Ultrasonography* 2020 ;39(4):356–66.
2. Du Y, Fang Z, Jiao BJ, Xi G, Zhu C, Ren Y, *et al.* Application of ultrasound-based radiomics technology in fetal lung texture analysis in pregnancies complicated by gestational diabetes or pre-eclampsia. *Ultrasound Obstet Gynecol* 2021;57(5):804–12.
3. Wei Y, Gao F, Zheng D, Huang Z, Wang M, Hu F, *et al.* Intrahepatic cholangiocarcinoma in the setting of HBV-related cirrhosis: Differentiation with hepatocellular carcinoma by using Intravoxel incoherent motion diffusion-weighted MR imaging. *Oncotarget* 2018;9(8):7975–83.
4. Wu W, Chen J, Bai C, Chi Y, Du Y, Feng S, *et al.* The Chinese guidelines for the diagnosis and treatment of pancreatic neuroendocrine neoplasms (2020). *Zhonghua Wai Ke Za Zhi* 2021;59(6):401–21.
5. Malone CD, Fetzer DT, Monsky WL, Itani M, Mellnick VM, Velez PA, *et al.* Contrast-enhanced US for the interventional radiologist: Current and emerging applications. *Radiographics* 2020;40(2):562–88.
6. Fattovich G, Giustina G, Schalm SW, Hadziyannis S, Sanchez-Tapias J, Almasio P, *et al.* Occurrence of hepatocellular carcinoma and decompensation in western European patients with cirrhosis type B. The EUROHEP study group on hepatitis B virus cirrhosis. *Hepatology* 1995;21(1):77–82.
7. Bravo AA, Sheth SG, Chopra S. Liver biopsy. *N Engl J Med* 2001;344(7):495–500.
8. Regev A, Berho M, Jeffers LJ, Milikowski C, Molina EG, Pylsopoulos NT, *et al.* Sampling error and intraobserver variation in liver biopsy in patients with chronic HCV infection. *Am J Gastroenterol* 2002;97(10):2614–8.
9. Foucher J, Chanteloup E, Vergniol J, Castera L, Le Bail B, Adhoute X, *et al.* Diagnosis of cirrhosis by transient elastography (FibroScan): a prospective study. *Gut* 2006;55(3):403–8.
10. Ganne-Carrié N, Ziol M, de Ledinghen V, Douvin C, Marcellin P, Castera L, *et al.* Accuracy of liver stiffness measurement for the diagnosis of cirrhosis in patients with chronic liver diseases. *Hepatology* 2006;44(6):1511–7.
11. Kazemi F, Kettaneh A, N'kontchou G, Pinto E, Ganne-Carrié N, Trinchet JC, *et al.* Liver stiffness measurement selects patients with cirrhosis at risk of bearing large oesophageal varices. *J Hepatol* 2006;45(2):230–5.

12. Kim BK, Han KH, Park JY, Ahn SH, Kim JK, Paik YH, *et al.* A liver stiffness measurement-based, noninvasive prediction model for high-risk esophageal varices in B-viral liver cirrhosis. *Am J Gastroenterol* 2010;105(6):1382–90.
13. Jung KS, Kim SU, Ahn SH, Park YN, Kim DY, Park JY, *et al.* Risk assessment of hepatitis B virus-related hepatocellular carcinoma development using liver stiffness measurement (FibroScan). *Hepatology* 2011;53(3):885–94.
14. Harrison SA. Utilization of FibroScan testing in hepatitis C virus management. *Gastroenterol Hepatol (N Y)* 2015;11(3):187–9.
15. Arthur R, Imam I, Saad M, Hackbart B, Mossad S. HCV in Egypt in 1977. *Lancet* 1995;346(8984):1239–40.
16. Anjum S, Ali S, Ahmad T, Afzal MS, Waheed Y, Shafi T, Ashraf M, Andleeb S. Sequence and structural analysis of 3'untranslated region of hepatitis C virus, genotype 3a, from Pakistani isolates. *Hepat Mon* 2013;13(5):e8390.
17. Köse Ş, Kuzucu L, Gözaydın A, Yilmazer T. Prevalence of hepatitis B and C viruses among asylum seekers in Izmir. *J Immigr Minor Health* 2015;17(1):76–8.
18. Gasim GI, Murad IA, Adam I. Hepatitis B and C virus infections among pregnant women in Arab and African countries. *J Infect Dev Ctries* 2013;7(8):566–78.
19. Noubiap JJ, Joko WY, Nansseu JR, Tene UG, Siaka C. Sero-epidemiology of human immunodeficiency virus, hepatitis B and C viruses, and syphilis infections among first-time blood donors in Edéa, Cameroon. *Int J Infect Dis* 2013;17(10):e832–7.
20. Waheed Y, Shafi T, Safi SZ, Qadri I. Hepatitis C virus in Pakistan: a systematic review of prevalence, genotypes and risk factors. *World J Gastroenterol* 2009;15(45):5647–53.
21. Muzaffar F, Hussain I, Haroon TS. Hepatitis C: the dermatologic profile. *J Pak Assoc Dermatol* 2008;18(3):171–81.
22. Yosry A, Fouad R, Alem SA, Elsharkawy A, El-Sayed M, Asem N, *et al.* FibroScan, APRI, FIB4, and GUCI: Role in prediction of fibrosis and response to therapy in Egyptian patients with HCV infection. *Arab J Gastroenterol* 2016;17(2):78–83.
23. Pradat P, Voirin N, Tillmann HL, Chevallier M, Trepo C. Progression to cirrhosis in hepatitis C patients: an age-dependent process. *Liver Int* 2007;27(3):335–9.
24. Alboraie M, Khairy M, Elsharkawy M, Asem N, Elsharkawy A, Esmat G. Value of Egy-Score in diagnosis of significant, advanced hepatic fibrosis and cirrhosis compared to aspartate aminotransferase-to-platelet ratio index, FIB-4 and Forns' index in chronic hepatitis C virus. *Hepatol Res* 2015;45(5):560–70.
25. Papastergiou V, Tsochatzis E, Burroughs AK. Non-invasive assessment of liver fibrosis. *Ann Gastroenterol* 2012;25(3):218–31.
26. Marcellin P, Ziol M, Bedossa P, Douvin C, Poupon R, de Ledinghen V, *et al.* Non-invasive assessment of liver fibrosis by stiffness measurement in patients with chronic hepatitis B. *Liver Int* 2009;29(2):242–7.
27. Castéra L, Vergniol J, Foucher J, Le Bail B, Chanteloup E, Haaser M, *et al.* Prospective comparison of transient elastography, Fibrotest, APRI, and liver biopsy for the assessment of fibrosis in chronic hepatitis C. *Gastroenterology* 2005;128(2):343–50.
28. Sandrin L, Fourquet B, Hasquenoph JM, Yon S, Fournier C, Mal F, *et al.* Transient elastography: a new noninvasive method for assessment of hepatic fibrosis. *Ultrasound Med Biol* 2003;29(12):1705–13.
29. Adhoue X, Foucher J, Laharie D, Terrebbonne E, Vergniol J, Castéra L, *et al.* Diagnosis of liver fibrosis using FibroScan and other noninvasive methods in patients with hemochromatosis: a prospective study. *Gastroenterol Clin Biol* 2008;32(2):180–7.
30. Kelleher T, MacFarlane C, de Ledinghen V, Beaugrand M, Foucher J, Castera L, *et al.* Risk factors and hepatic elastography (FibroScan) in the prediction of hepatic fibrosis in non-alcoholic steatohepatitis. *Gastroenterology*. 2006;130(4):A768.
31. Ziol M, Handra-Luca A, Kettaneh A, Christidis C, Mal F, Kazemi F, *et al.* Noninvasive assessment of liver fibrosis by measurement of stiffness in patients with chronic hepatitis C. *Hepatology* 2005;41(1):48–54.
32. Ogawa E, Furusyo N, Toyoda K, Takeoka H, Otaguro S, Hamada M, *et al.* Transient elastography for patients with chronic hepatitis B and C virus infection: Non-invasive, quantitative assessment of liver fibrosis. *Hepatol Res* 2007;37(12):1002–10.
33. Corpechot C, El Naggari A, Poujol-Robert A, Ziol M, Wendum D, Chazouillères O, *et al.* Assessment of biliary fibrosis by transient elastography in patients with PBC and PSC. *Hepatology* 2006;43(5):1118–24.
34. Sporea I, Sirlin R, Deleanu A, Tudora A, Curescu M, Cornianu M, *et al.* Comparison of the liver stiffness measurement by transient elastography with the liver biopsy. *World J Gastroenterol* 2008;14(42):6513–7.
35. Yoneda M, Yoneda M, Mawatari H, Fujita K, Endo H, Iida H, *et al.* Noninvasive assessment of liver fibrosis by measurement of stiffness in patients with nonalcoholic fatty liver disease (NAFLD). *Dig Liver Dis* 2008;40(5):371–8.
36. Kim KM, Choi WB, Park SH, Yu E, Lee SG, Lim YS, *et al.* Diagnosis of hepatic steatosis and fibrosis by transient elastography in asymptomatic healthy individuals: a prospective study of living related potential liver donors. *J Gastroenterol* 2007;42(5):382–8.
37. Berends MA, Snoek J, de Jong EM, Van Krieken JH, de Knegt RJ, van Oijen MG, *et al.* Biochemical and biophysical assessment of MTX-induced liver fibrosis in psoriasis patients: Fibrotest predicts the presence and Fibroscan predicts the absence of significant liver fibrosis. *Liver Int* 2007;27(5):639–45.
38. Luşor M, Badea R, Stefănescu H, Grigorescu M, Sparchez Z, Serban A, *et al.* Analysis of histopathological changes that influence liver stiffness in chronic hepatitis C. Results from a cohort of 324 patients. *J Gastrointestin Liver Dis* 2008;17(2):155–63.
39. Coco B, Oliveri F, Maina AM, Ciccorossi P, Sacco R, Colombaro P, *et al.* Transient elastography: a new surrogate marker of liver fibrosis influenced by major changes of transaminases. *J Viral Hepat* 2007;14(5):360–9.
40. Friedrich-Rust M, Ong MF, Martens S, Sarrazin C, Bojunga J, Zeuzem S, *et al.* Performance of transient elastography for the staging of liver fibrosis: a meta-analysis. *Gastroenterology* 2008;134(4):960–74.
41. Castera L, Le Bail B, Foucher J, Bertet J, Darriet M, Couzigou P, *et al.* Prospective analysis of discordance between FibroScan and FibroTest when used in combination as first-line assessment of liver fibrosis in chronic hepatitis C. *Hepatology* 2005;42(Suppl 1):440A.
42. Blanc PL, Gabbuti A, Marino N, Mecocci L, Mazzotta F. Liver stiffness in chronic hepatitis C: will it modify the assessment of patients? *J Hepatol* 2007;46(Suppl 1):S201–2.
43. Seo YS, Kim ES, Kwon YD, Park S, Keum B, Park BJ, *et al.* Liver stiffness measurement in patients with chronic hepatitis B is not as useful as that in patients with chronic hepatitis C for the assessment of liver fibrosis. *Hepatology*. 2007;46(Suppl 4):842A.

Submitted: July 20, 2022

Revised: December 8, 2022

Accepted: December 8, 2022

Address for Correspondence:**Muhammad Arshad**, The Institute of Nuclear Medicine, Oncology and Radiotherapy (INOR), Abbottabad-Pakistan**Cell:** +92 300 911 0632**Email:** arshad_ath@yahoo.com