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Short Communication **Open Access**

Relationship between serum viral load and stages of hepatic fibrosis in patients with chronic hepatitis C virus infections in Plateau State, Nigeria

[1,2,3]Maktep, Y, D., [1,2]Egah, D. Z., and [1]Nimzing, L.

[1]Department of Medical Microbiology, Faculty of Clinical Sciences, College of Health Sciences, University of Jos, PMB 2084 Jos, Nigeria
[2]Department of Medical Microbiology, Jos University Teaching Hospital, Jos, Nigeria
[3]Department of Medical Microbiology and Parasitology, College of Health Sciences, Bingham University, Jos Campus, Nigeria
*Correspondence to: yadangmaktep@gmail.com

Abstract

Background: Chronic hepatitis C virus (HCV) infection is a major cause of chronic liver disease worldwide and remains a significant contributor to liver-related morbidity and mortality. Hepatic fibrosis is the key determinant of long-term clinical outcomes. Although viral replication is central to HCV pathogenesis, the association between serum HCV load and the severity of hepatic fibrosis remain controversial. The objective of this study is to evaluate the relationship between serum HCV load and hepatic fibrosis severity, using Transient Elastography (FibroScan), among patients with chronic HCV infection.
Methodology: A descriptive cross-sectional study with longitudinal follow up of confirmed cases was conducted among 40 adults with confirmed chronic HCV infection (HCV-RNA positive). Serum viral load was quantified using real-time reverse-transcription polymerase chain reaction (rt RT-PCR) assay. Hepatic fibrosis was assessed non-invasively using FibroScan, and liver stiffness measurements (LSM) were categorized according to METAVIR-equivalent cut-offs of F0 (<5.5 kPa), F1 (5.5–7.0 kPa), F2 (7.1–9.5 kPa), F3 (9.6–12.5 kPa), and F4 (>12.5 kPa). Spearman's correlation coefficient was used to determine the association between viral load and fibrosis severity as the data deviated significantly from the normality.
Results: The mean age of participants was 56.10±15.73 years with a male-to-female ratio of 4:1. Liver stiffness values ranged from 4.7 to 35.8 kPa, while serum viral load varied widely (20,100 to 680,000 IU/mL). Most participants had early-stage fibrosis (F0–F1, 70%). A weak positive correlation was observed between serum viral load and liver stiffness measurements (r=0.139), that was not statistically significant (p=0.391).
Conclusion: Serum HCV load showed no significant association with hepatic fibrosis severity. These findings indicate that viral load alone is a poor predictor of fibrosis progression and underscore the clinical value of Transient Elastography for routine assessment of liver disease in patients with chronic HCV infection.

Keywords: HCV; viral load; hepatic fibrosis; FibroScan

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Relation entre la charge virale sérique et les stades de fibrose hépatique chez les patients atteints d'une infection chronique par le virus de l'hépatite C dans l'État de Plateau, au Nigéria

[1,2,3]Maktep, Y. D., [1,2]Egah, D. Z., et [1]Nimzing, L.

[1]Département de Microbiologie Médicale, Faculté des Sciences Cliniques, Collège des Sciences de la Santé, Université de Jos, PMB 2084 Jos, Nigéria
[2]Département de Microbiologie Médicale, Centre Hospitalier Universitaire de Jos, Jos, Nigéria
[3]Département de Microbiologie Médicale et de Parasitologie, Collège des Sciences de la Santé, Université Bingham,

Campus de Jos, Nigéria
*Correspondance à: yadangmaktep@gmail.com

Résumé:

Contexte: L'infection chronique par le virus de l'hépatite C (VHC) est une cause majeure de maladie hépatique chronique dans le monde et contribue de manière significative à la morbidité et à la mortalité liées au foie. La fibrose hépatique est le principal déterminant des résultats cliniques à long terme. Bien que la réplication virale soit essentielle à la pathogenèse du VHC, l'association entre la charge virale sérique du VHC et la sévérité de la fibrose hépatique reste controversée. L'objectif de cette étude est d'évaluer la relation entre la charge virale sérique du VHC et la sévérité de la fibrose hépatique, par élastographie impulsionnelle (FibroScan), chez des patients atteints d'une infection chronique par le VHC.
Méthodologie: Une étude descriptive transversale avec suivi longitudinal des cas confirmés a été menée auprès de 40 adultes atteints d'une infection chronique confirmée par le VHC (ARN du VHC positif). La charge virale sérique a été quantifiée par RT-PCR en temps réel. La fibrose hépatique a été évaluée de manière non invasive par FibroScan, et les mesures de rigidité hépatique (MRH) ont été classées selon les seuils équivalents à ceux de METAVIR: F0 (< 5,5 kPa), F1 (5,5–7,0 kPa), F2 (7,1–9,5 kPa), F3 (9,6–12,5 kPa) et F4 (> 12,5 kPa). Le coefficient de corrélation de Spearman a été utilisé pour déterminer l'association entre la charge virale et la gravité de la fibrose, car les données s'écartaient significativement de la normalité.
Résultats: L'âge moyen des participants était de 56,10±15,73 ans, avec un ratio hommes/femmes de 4/1. Les valeurs de rigidité hépatique variaient de 4,7 à 35,8 kPa, tandis que la charge virale sérique présentait une grande variabilité (de 20 100 à 680 000 UI/mL). La plupart des participants présentaient une fibrose à un stade précoce (F0–F1, 70%). Une faible corrélation positive a été observée entre la charge virale sérique et les mesures de rigidité hépatique (r=0,139), mais cette corrélation n'était pas statistiquement significative (p=0,391).
Conclusion: La charge virale sérique du VHC n'a montré aucune association significative avec la sévérité de la fibrose hépatique. Ces résultats indiquent que la charge virale seule est un mauvais prédicteur de la progression de la fibrose et soulignent l'intérêt clinique de l'élastographie impulsionnelle pour l'évaluation de routine des maladies hépatiques chez les patients atteints d'une infection chronique par le VHC.

Mots-clés: VHC; charge virale; fibrose hépatique; FibroScan

Introduction:

Hepatitis C virus (HCV) infection is a leading cause of chronic liver disease worldwide, which may progress to liver fibrosis, cirrhosis, and hepatocellular carcinoma if untreated (1,2, 3,4). The extent of hepatic fibrosis is a critical determinant of prognosis, therapeutic decision-making, and long-term patient monitoring (2, 5). Historically, liver biopsy served as the 'gold standard' for fibrosis assessment, however, its invasive nature, sampling variability and potential complications have limited its routine use (6,7). Consequently, non-invasive methods such as Transient Elastography (FibroScan), have gained widespread acceptance due to their safety, reproducibility, and strong correlation with histological fibrosis stages (5,8,9). Also, liver stiffness can be quantified as a continuous variable and can help physicians in grading the severity of hepatic fibrosis in order to estimate the likelihood of developing liver related complications including hepatocellular carcinoma (10,11,12).

The clinical relevance of quantitative serum HCV-RNA levels in predicting severity of hepatic fibrosis remains uncertain (4). While viral replication is essential for disease initiation and persistence, studies have reported inconsistent associations between viral load and fibrosis progression (13,14). There is increasing evidence to suggest that host-related factors, including immune response, duration of infection, metabolic comorbidities, alcohol consumption, and age, may exert a greater influence on fibrogenesis than circulating viral RNA levels alone (13,15).

In resource-limited settings, clinicians often rely on readily available laboratory parameters such as viral load for risk stratification. Clarifying the relationship between serum viral load and hepatic fibrosis is therefore of practical clinical importance. This study aimed to evaluate the association of serum HCV load on hepatic fibrosis severity using FibroScan as a non-invasive assessment tool.

Materials and method:

Study design and setting:

This was a descriptive cross-sectional study of adult patients (18 years and above) with suspected hepatitis, and a longitudinal follow up of confirmed cases, in 9 selected Primary Healthcare Centers (PHCs) within the 3 senatorial districts of Plateau State, Nigeria.

Ethical consideration:

Ethical approval was obtained from the Health Research Ethics Committee of Plateau State Specialist Hospital (NHREC/09/23/2010b),

Jos, Nigeria. Written informed consent was obtained from all participants prior to enrollment, and the study was conducted in accordance with the Declaration of Helsinki

Study population and sample size

The study population were adult patients (18 years and above) with suspected hepatitis attending the general outpatient departments (GOPD) of the selected PHCs. The minimum sample size was calculated using the formula described by Araoye (16), $n=Z^2pq/d^2$ where N=minimum sample size, Z= standard normal deviation corresponding to 95% levels of significance (=1.96), p=prevalence rate of HCV of 18.4% (0.184) in the study by Uchendu et al., (17), q=1-p and d is the degree of accuracy desired, set at 5% (0.05). This gave a calculated sample size of 231, which was adjusted for 15% attrition to 266, but a total of 461 participants were recruited to increase the power of the study.

Selection criteria and method of sampling:

The inclusion criteria included patients aged 18 years and above who consented to participate in the study and without prior knowledge of their HCV status. Patients less than 18 years of age and those with history of confirmed HCV infection were excluded.

The local government areas and PHCs within each of the senatorial zones were selected by simple random sampling. The patients presenting to GOPD of the PHCs who consented to participate in the study were recruited by simple random sampling technique until the sample size was reached.

Data and sample collection:

Data on socio-demographic characteristics from each participant were collected using a structured, interviewer-administered questionnaire. Five milliliters of venous blood were collected aseptically from each participant into EDTA vacutainer. Plasma was separated by centrifugation at 2000 rpm for 5 minutes and stored at −20°C until laboratory analysis.

Preliminary screening for HCV by ELISA and confirmation by PCR:

Preliminary screening of all 461 participants for HCV antibodies was done by the Enzyme Linked Immunosorbent Assay (ELISA kit, DIAPRO Diagnostics, Italy). Forty-nine participants positive for HCV antibodies were confirmed HCV-RNA positive using HCV-RNA PCR (Luna PCR kit, New England BioLabs, Germany), and after a minimum follow-up period of six months, 40 participants were successfully enrolled for quantitative viral load analysis and fibrosis assessment.

Quantitative HCV load testing:

HCV-RNA quantification was performed using the Bosphore® HCV Quantification Kit on the Bio-Rad CFX96 Real-Time PCR system in accordance with the manufacturer's instructions. Viral RNA extraction was carried out using the Quick Viral RNA Extraction Spin Kit. Results were expressed in IU/mL.

Hepatic fibrosis assessment:

Hepatic fibrosis was assessed using Transient Elastography (FibroScan). Liver stiffness measurements were recorded in kilopascals (kPa) and categorized according to METAVIR-equivalent cut-offs: F0 (<5.5 kPa), F1 (5.5–7.0 kPa), F2 (7.1–9.5 kPa), F3 (9.6–12.5 kPa), and F4 (>12.5 kPa) (18).

Statistical analysis:

Data were analyzed using descriptive statistics. Normality test was assessed using Kolmogorov-Smirnov and Shapiro–Wilk tests. Spearman's rank correlation coefficient was applied to evaluate the relationship between serum viral load and liver stiffness measurements since the variables were not normally distributed. Statistical significance was set at $p<0.05$.

Results:

Socio-demographic and clinical characteristics of the study participants:

Table 1 shows the sociodemographic and clinical characteristics of the 40 enrolled study participants. The mean age of the participants was 56.10±15.73 years, with 80% males and 20% females. Majority of the participants were in the age groups 40–49 years and 50-59 years, accounting for 40% each of the study population.

The liver fibrosis assessment using FibroScan showed that the highest frequency of participants had stage F_1 fibrosis (40.0%), followed by stage F_0 (30.0%), while the lowest frequencies of the participants were classified as F_2, F_3 and F_4, accounting for 10% each. The FibroScan scores ranged from 4.7 to 38.8 Kpa (Kilopascal). The HCV load ranged from 20,100 to 680,000 IU/mL.

Table 1: Socio-demographic and clinical characteristics of the study participants

Variables	Frequency	Percentage
Age group (years)		
40-49	16	40.0
50-59	16	40.0
≥60	8	20.0
Mean age (± SD)	56.10 ± 15.73	
Gender		
Male	32	80.0
Female	8	20.0
FibroScan stage		
F_0	12	30.0
F_1	16	40.0
F_2	4	10.0
F_3	4	10.0
F_4	4	10.0

Table 2 shows association between age, gender and hepatic fibrosis among the participants. There was a statistically significant association between age and stages of hepatic fibrosis (x^2=34.164, p=0.001) with early-stage fibrosis (F0, F1) being significantly commoner in middle age (40-49 years age group) while late-stage fibrosis (F2, F3, F4) was commoner in older adults (>50 years of age). However, there was no significant association between gender and stages of hepatic fibrosis (x^2=4.58, p=0.333).

Table 3 shows the assessment result of the normality distribution of the variables (FibroScan scores and HCV load) using Kolmogo rov–Smirnov and Shapiro wilk tests. Both FibroScan scores and HCV load significantly deviated from normal distribution (p=0.001 for both), which necessitated the use of Spearman's correlation.

Table 4 shows the Spearman's correlation between HCV load and stages of hepatic fibrosis. A weak positive correlation was observed between HCV load and stages of hepatic fibrosis (r=0.139), which was not statistically significant (p=0.391).

Table 2: Relationship between stages of hepatic fibrosis and demographic characteristics of the participants

Demographic characteristics	Stages of hepatic fibrosis					Total	χ^2	*p* value
	F_0	F_1	F_2	F_3	F_4			
Age group (years)								
40-49	8 (50.0)	8 (50.0)	0	0	0	16	34.167	0.001
50-59	4 (25.0)	4 (25.0)	0	4 (25.0)	4 (25.0)	16		
≥60	0	4 (50.0)	4 (50.0)	0	0	8		
Gender								
Male	8 (25.0)	12 (37.5)	4 (12.5)	4 (12.5)	4 (12.5)	32	4.583	0.333
Female	4 (50.0)	4 (50.0)	0	0	0	8		

Table 3: Tests of normality for HCV load and liver stiffness measurement

Parameter	Kolmogorov-Smirnov			Shapiro-Wilk		
	Statistic	df	*p* value	Statistic	Df	*p* value
HCV load	0.200	40	0.001	0.864	40	0.001
FibroScan score	0.360	40	0.001	0.478	40	0.001

df = degree of freedom; HCV = Hepatitis C virus

Table 4: Spearman correlation analysis between serum HCV load and hepatic FibroScan score

			HCV load	FibroScan score
Spearman's rho	**HCV load**	Correlation coefficient	1	0.139
		p value		0.391
		Number	40	40
				1
	FibroScan score	Correlation coefficient	0.139	
		p value	0.391	
		Number	40	40

HCV = Hepatitis C virus

Discussion:

The study evaluated the correlation between serum HCV load and hepatic fibrosis severity assessed using transient Elastography (FibroScan) among the participants with confirmed chronic HCV infection. The findings showed that there was no statistically significant association between HCV load and the severity of hepatic fibrosis. Although, a weak positive correlation was observed between HCV load and liver stiffness measurement (FibroScan score), the correlation was not statistically significant, suggesting that serum HCV load alone may not be a reliable predictor for progression of liver fibrosis in chronic HCV infected patients.

The sociodemographic characteristics of the study participants revealed that most were middle-aged aged (40-49 years) and older adults (50-59 years), indicating that prevalence of HCV infections are higher in middle age and older adults in the study population. This finding is consistent with the natural history of chronic HCV infection in which the fibrosis of the liver develops progressively over many years before clinical manifestation occurs (7,19). This finding is similar to previous reports by other researchers (7,20). The predominance of male participants in this study may be related to increased exposure to occupational and behavioral risk factors associated with bloodborne viral infections.

Notably, 10% of the participants already had stage 4 (F4) fibrosis despite having no prior knowledge of their HCV status. This suggests that many individuals in the community in Plateau State remains unaware of their HCV status and may eventually presents with severe complication in healthcare facilities. This finding is in tandem with previous reports by Pandey and co-workers (21) that many individuals in the community are unaware of their HCV status and remain undiagnosed until complications become evident. Forty percent of the participants were found with mild fibrosis (F1) which may be due to early detection or variation in the progression of HCV infection among the participants.

The serum HCV load and liver stiffness measurement values (FibroScan scores) both shows wide variability among the study population reflecting heterogeneity in viral replication activity and the severity of the HCV infection. A statistically significant association was observed between age and stages of fibrosis, with higher frequency of advanced fibrosis observed among older age group (50-59 years) compared to younger age group (40-49 years). This finding agrees with previous reports by Zeremski et al., (2) and Arshad & coworkers (7), and may be attributed to prolong duration of infection, cumulative hepatic injury over time and/or decline in hepatic regenerative activity with advancing age. The association between gender and stages of hepatic fibrosis was not statistically significant although males were more represented across the fibrosis stages compared to female participants. The lack of significance may be due to relatively small sample size.

The normality tests revealed that both FibroScan scores and HCV load were not normally distributed. The significant deviation from normality could be attributed to the wide variation in HCV load and FibroScan scores seen among the participants. By Spearman's rank correlation analysis, there was weak correlation coefficient (r=0.139) between HCV load and severity of liver fibrosis, which was not statistically significant (p=0.391). This implies that increasing HCV load does not necessarily correspond to worsening of liver fibrosis. HCV load reflects viral replication activities and not necessarily the degree of hepatic structural damage. This finding suggests that hepatic injury and fibrogenesis in chronic HCV infection may be influenced by host immune responses and other clinical or metabolic factors than by circulating RNA level alone (13,14). The predominance of early-stage fibrosis observed in this study despite markedly elevated viral load in some patients further strengthens this observation.

These findings agree with those of other studies that reported no significant correlation between serum HCV load and severity of hepatic fibrosis (13,14). However, some studies have reported contrasting findings of significant correlation between serum HCV load and hepatic fibrosis severity (4,7). The discrepancies across studies may be explained by differences in study design, population characteristics, viral genotypes, duration of infection and environmental or genetic factors such as obesity, alcohol use, viral coinfection and insulin resistance.

The finding of this study has important clinical implications especially in resource-limited settings where HCV load determination may often be interpreted as indicator of HCV disease severity. While the HCV load remains an important aspect in confirming active infection and monitoring treatment, this study suggest that it should not be used independently to predict severity of hepatic fibrosis. Assessing hepatic fibrosis using FibroScan remains an important tool for the evaluation of hepatic fibrosis and guiding clinical management in

patients with chronic HCV infection.

This study is limited by relatively small sample size, which limits the generalizability of the findings. The cross-sectional design also precludes causal inference between viral load and fibrosis progression. Additionally, liver biopsy, the histological 'gold standard' was not performed; however, the FibroScan used is a validated and widely accepted non-invasive alternative. Furthermore, information on viral genotype, duration of infection, alcohol consumption, and metabolic comorbidities was limited and may have influenced fibrosis severity.

Conclusion:

In this study, serum HCV load was not significantly associated with hepatic fibrosis severity and should therefore not be used in isolation to predict fibrosis progression. Transient Elastography (FibroScan) remains a valuable non-invasive tool for fibrosis assessment, particularly in resource-limited settings. Future studies incorporating intrahepatic viral replication and immunologic markers are recommended to further elucidate determinants of fibrosis progression in chronic HCV infection.

Contributions of authors:

MY conceived and designed the study, coordinated data collection and laboratory analyses, performed FibroScan assessments, and contributed to data interpretation. EZD and NL provided supervision and critical intellectual input. All authors contributed to manuscript drafting, reviewed the final version, and approved the manuscript for submission.

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Conflicts of interest:

Authors declare no conflicts of interest.

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