

ORIGINAL ARTICLE



Liver Fibrosis Assessment using Transient Elastography among Chronic Hepatitis B Patients in Jos, North Central Nigeria

Obekpa Solomon¹, Bello Ruth², Malu Abraham¹

Abstract

Background: Liver fibrosis assessment is crucial for clinical management of chronic hepatitis B (CHB) patients, to predict prognosis, therapeutic decisions and long-term monitoring. It is important to have an early diagnosis of liver cirrhosis in CHB patients because cirrhosis is an independent predictor of mortality. Similarly, early diagnosis and staging of fibrosis are very important considering current evidence that prompts initiation of fibrosis treatment and that of the underlying cause could halt progression to cirrhosis and HCC and enhance its reversal or resolution. It is therefore important that every CHB patient has an initial fibrosis assessment and subsequently for monitoring of disease progression or response to treatment.

Objective: To assess the prevalence of liver fibrosis among CHB patients in Jos, using transient elastography.

Methodology: This was a hospital-based cross-sectional study, where 120 CHB adult patients attending the gastroenterology clinic were consecutively recruited. A questionnaire was used to seek information from the subjects. Transient elastography was done for all participants, and the data obtained were analysed using SPSS version 25.

Results: The mean study age of participants was 36±12 years, with 69 (57.5%) females and 51 (42.5%) males. There was no or minimal fibrosis (F0/F1) in 73.3%, and significant fibrosis (≥F2) in 26.7%. Increasing age, lack of formal education, rural residence, and female gender were all associated with liver fibrosis (p=0.001, 0.001, 0.001 and 0.024, respectively)

Conclusion: A significant fibrosis of 26.7% among asymptomatic CHB patients demonstrates the need for fibrosis assessment for every patient with CHB, even without symptoms.

Key words

Liver fibrosis, Transient elastography, Chronic hepatitis B, Jos, Prevalence

Introduction

Liver fibrosis refers to the excessive accumulation of extracellular matrix proteins, including collagen, that occurs in most types of chronic liver diseases. This condition results from the liver's healing response to chronic injury.^{1,2} Chronic hepatitis B (CHB) is a major cause of liver fibrosis and cirrhosis, both of which are independent risk factors for

hepatocellular carcinoma (HCC). Notably, 70–90% of HCC cases among individuals with CHB occur in individuals with underlying liver cirrhosis.³ Liver fibrosis serves as an indicator of poor clinical outcomes and can progress to liver cirrhosis (an advanced stage of liver fibrosis) along with its complications and HCC.⁴

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Assessment for liver fibrosis is essential for the effective clinical management of CHB patients, as it aids in predicting prognosis, guiding therapeutic decisions, and long-term monitoring¹. Early diagnosis of liver cirrhosis in patients with chronic hepatitis B (CHB) is crucial, as cirrhosis is an independent predictor of both morbidity and mortality.^{1,5} Likewise, early diagnosis and staging of fibrosis are very important considering current evidence that prompt initiation of fibrosis treatment and that of the underlying cause could halt progression to cirrhosis and HCC and also, enhance its reversal.^{6,7,1} It is, therefore, important that every CHB patient has an initial fibrosis assessment and subsequently for monitoring of disease progression or response to treatment.

In Nigeria, there have been limited studies evaluating the prevalence of liver fibrosis among patients with hepatitis B virus (HBV) infection.⁷ This scarcity of research may be attributed to the challenges associated with the invasive nature of liver biopsy, which remains the gold standard for the assessment of liver fibrosis. However, transient elastography has emerged as an excellent non-invasive alternative with an excellent performance in predicting significant fibrosis and even higher accuracy in identifying liver cirrhosis.⁵ It measures liver stiffness using a FibroScan machine, which is a well-validated method with advantages of a short procedure time (<5 min), immediate results, and the ability to perform the test at the bedside or in an outpatient clinic.⁸

In addition to transient elastography, serum indices such as the Fibrosis-4 (FIB-4) index and the Aspartate Platelet Ratio Index (APRI) score are also recommended as non-invasive alternatives, especially in resource-constrained environments where access to FibroScan technology may be limited or where cost considerations are of significant concern.⁹

OBJECTIVE

This study aims to assess the prevalence of liver fibrosis among chronic hepatitis B patients in Jos, using transient elastography.

METHODOLOGY

Study design

This was a hospital-based cross-sectional study.

Study site and population

This study was carried out in the gastroenterology outpatient clinic of the Jos University Teaching Hospital (JUTH), Jos. Jos is the capital of Plateau State, located in North-central Nigeria. Subjects aged 18 years and above diagnosed of chronic HBV infection by a positive hepatitis B surface antigen (HBsAg) for six months or more with the presence of hepatitis B core antibody (HBcAb) immunoglobulin G (IgG), who presented at the adult gastroenterology clinic in JUTH and met the inclusion criteria constituted the study population.

Sample Size Determination

The sample size for this study was calculated using Bennett and Fisher's formula.

$$N = \frac{Z^2 \times p(1-p)}{d^2}$$

Where

N represents the minimum required sample size
Z² is the standard normal deviate at a 95% confidence level, usually given as 1.96

P is the estimated prevalence of chronic hepatitis B virus (HBV) infection in Nigeria, which has been reported to be 8.1%¹⁰

d is the desired level of precision, set at 5% (0.05) for this study.

Substituting these values yields:

$$N = (1.96)^2 \times 0.081 \times (1 - 0.081) / (0.05)^2 \approx 114$$

a total of 120 participants were ultimately recruited for the study.

Inclusion and Exclusion Criteria

Participants were eligible for inclusion if they were Nigerian adults aged 18 years or older, with a confirmed diagnosis of chronic hepatitis B infection.

Participants were excluded from the study if they were under 18 years of age, had ultrasound evidence of hepatic masses suggestive of liver tumours, or had confirmed HCC. Additional exclusion criteria included lack of consent to participate, co-infection with HIV and/or hepatitis C virus (HCV), and a history of significant alcohol consumption—defined as intake exceeding 14 units per week for females or 21 units per week for males. Pregnant women were excluded, as were individuals with ascites, those exhibiting features suggestive of variceal bleeding (such as melena, hematochezia, or hematemesis), those with signs of hepatic encephalopathy, and individuals with a body mass index (BMI) ≥ 30 kg/m².

Ethical clearance/approval

Ethical approval for the study was obtained from the Health Research Ethics Committee of JUTH on the 3rd February, 2021 (JUTH/DCS/IREC/XXXI/2381).

Sampling technique

A convenience sampling method was adopted where consecutive patients attending the gastroenterology clinic at the Jos University Teaching Hospital who had a confirmed diagnosis of chronic hepatitis B virus (HBV) infection and met the predefined inclusion criteria, were consecutively recruited until the target sample size of 120 participants was achieved. Data collection was carried out using a structured questionnaire, and liver stiffness measurement was performed by one of the researchers for all the participants using M-mode images obtained with a fibroscan machine (Echosens, Paris, France).

Materials

The materials utilised for this study included a structured questionnaire used to collect demographic and clinical data from participants. Liver stiffness measurements were performed using a FibroScan machine (Echosens, Paris, France), with the aid of scanning gel to ensure proper contact and signal transmission. Tissue papers were used to clean residual gel post-procedure.

Anthropometric measurements were obtained using a stadiometer to measure height and a calibrated weighing scale for weight assessment. For blood sample collection, sterile needles and syringes, blood sample bottles, cotton wool, and methylated spirit were employed, ensuring standard aseptic techniques. Additionally, abdominal imaging was conducted using a GE Logiq V5 ultrasound

machine to assess liver morphology and exclude the presence of hepatic masses.

Study procedure

The purpose of the study was explained to each subject, and consent was obtained via a consent form. An interviewer-administered questionnaire was completed for each subject, seeking information about demographic data, previous history of hepatic decompensation and social history. A clinical examination was carried out with a focus on the weight and height of the subjects for the determination of BMI. All information obtained was treated as confidential.

FibroScan: Liver stiffness measurements were performed by FibroScan (Echosens, Paris, France) using an M probe on the right lobe of the liver through intercostal spaces on patients lying in the dorsal decubitus position with the right arm in maximal abduction. By pressing a button on the probe, a series of painless pulses is applied to the liver. Thus, generating an overall liver stiffness score, which is expressed in kilopascal (KPa) and corresponds to the median of 10 validated measurements. Subjects were assigned to different fibrosis stages according to their fibroscan score with the following cut-off values.

- F0/F1: 2.5 – 7.0 Kpa
- F2: 7.1 - 9.4 Kpa
- F3: 9.5 – 12.4 Kpa
- F4: 12.5 - 75 Kpa (Cirrhosis)

This was further classified thus: Stages F0/F1 = insignificant fibrosis, \geq F2 = significant fibrosis.

Abdominal Ultrasound Scan: Abdominal USS was performed with focus on the liver to determine the size, border, echotexture and to detect any possible mass or tumour that may be suggestive of malignancy, for exclusion from the study.

Statistical analysis

Data obtained were entered into an Excel sheet and subsequently analysed using SPSS version 25. Data were represented using descriptive statistics such as tables, graphs and bar charts. Categorical variables (like Gender, marital status, educational status, occupation, and residence) were expressed as proportions and percentages. Continuous variables with normal distribution (like age) were expressed as means \pm standard deviations or as ranges. Linear regression was used to test the association between quantitative variables (Age and Fibrosis score), while Chi-square was used for the test of significance between categorical variables. A p-value of < 0.05 was considered statistically significant.

RESULTS

A total of 120 subjects were recruited for this study. The results of the analysed data set for those who participated in the study are as shown below.

Socio-Demographic Characteristics of the Study Subjects (Table 1)

The age of the subjects ranged from 18 years to 66 years. The mean age was 36.8 (± 12) years. The study population was made up of 51 (42.5%) males and 69 (57.5%) females. The male to female ratio was 1:1.4. The majority (68.3%) of the subjects had tertiary education, 26 (21.7%) attained secondary level of education, 3 (2.5%) attained primary level of education, and 9 (7.5%) of the subjects had informal education only.

More than half of the subjects, 63 (52.5%) were married, 52 (43.3%) were single, while 5 (4.2%) were widows. Most of the subjects (34.2%) were students, and the least common occupation was farming (13.3%), while 21 (17.5%) were civil servants, business owners and other occupations respectively. The majority of the subjects (59.2%) were urban dwellers, while 49 (40.8%) resided in rural areas.

Table 1: Socio-demographic characteristics of the study population

Variables	Frequency (n= 120)	Percentage (%)
Age distribution:		
≤ 20	8	6.7
21-30	35	29.2
31-40	37	30.8
41-50	21	17.5
51-60	15	12.5
>60	4	3.3
Mean age: 36.12 (± 12)		
Gender		
Male	51	42.5
Female	69	57.5
Educational status		
Primary	3	2.5
Secondary	26	21.7
Tertiary	82	68.3
Informal	9	7.5
Marital status		
Married	63	52.5
Single	52	43.3
Widow	5	4.2
Occupation		
Civil servant	21	17.5
Business	21	17.5
Student	41	34.2
Farmer	16	13.3
Others	21	17.5
Residence		
Urban	71	59.2
Rural	49	40.8

Prevalence and stages of liver fibrosis based on liver stiffness measurement

Figure 1 shows the prevalence and categorisation (prevalence of different stages of fibrosis) of the subjects based on the different stages of liver fibrosis from liver stiffness measurement (bar chart). Most of the subjects, 88 (73.3%), had no significant fibrosis (F0/F1), while 10 (8.3%), 5 (4.2%) and 17 (14.2%) had F2, F3 and F4, respectively. Thirty-two (26.7%) participants had significant fibrosis (\geq F2) while 17 (14.2%) had cirrhosis (F4)

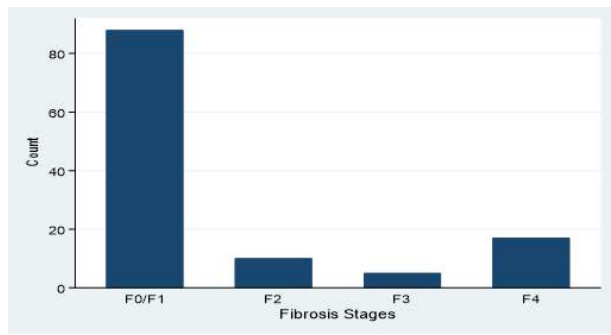


Figure 1 Categorisation of subjects into different categories of liver fibrosis stage.

Relationship between liver stiffness measurement (Fibrosis) and age of study subjects

The linear regression curve (Fig. 2) shows a direct proportional relationship between the ages of subjects and fibroscan score ($r=0.347$; $P<0.001$).

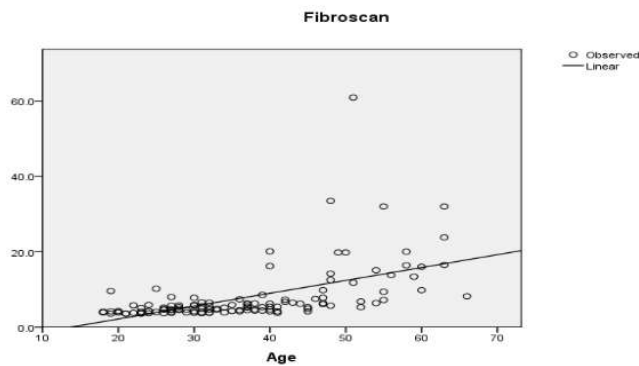


Figure 2: Linear regression curve between age and fibroscan score of study subjects

DISCUSSION

The study was carried out among 120 asymptomatic chronic hepatitis B subjects to determine the prevalence of liver fibrosis using liver stiffness measurement with a transient

elastography (FibroScan) machine.

The mean age of the subjects (36.81 ± 12) shows that the burden of liver disease from chronic hepatitis B infection in our environment occurs among the young age group. Similar demography has been reported by other studies in the past in same environment and other parts of Nigeria.^{12,13} A mean age of 29.82 years was reported by Ndububa et al¹² in their study among the asymptomatic subjects at Ile-Ife, while Ameh et al¹³ reported 36.3 years among their study subjects in Jos, Nigeria.

The lower mean age in this study could also be explained by reasons such as the opportunities for HBsAg screening in most patients seen at the clinic, which include pre-employment screenings, pre-marital screenings and during blood donations. This is of concern because this young age group contributes significantly to the workforce of any country.

The predominance of females in this study, with a male-to-female ratio of 1:1.4, is in contrast to some previous reports in Nigeria of higher hepatitis B prevalence among males.^{12,13} This can be accounted for by the exclusion of those with a significant history of alcohol consumption, who were predominantly males from our study. Alcohol consumption has been reported to be more common among males compared to females in Nigeria.¹⁴

Most of the subjects (68.3%) had a tertiary level of education; this is not surprising, as many young people in urban areas pursue tertiary education or white-collar jobs, given that most of the subjects are young urban dwellers.

The prevalence of significant liver fibrosis and cirrhosis was 26.7% and 14.2%, respectively, from this study. The prevalence of significant fibrosis in this study is similar those some previously reported by Ameh et al¹³ in Jos but higher than another report by Okeke et al¹⁵ also in Jos, where a small sample size far less than a hundred (forty seven) was used for the study and may have resulted to this contrary finding. The values from this study are, however, lower than the 56.6%

Table II: Association between fibrosis score and socio-demographic variables

Variable	Category	No Significant Fibrosis n (%)	Significant Fibrosis n (%)	Total	Chi-square (χ^2)	p-value
Age Group	< 20	8 (100.0)	0 (0.0)	8	23.410	0.001
	21–30	32 (91.4)	3 (8.6)	35		
	31–40	31 (83.8)	6 (16.2)	37		
	41–50	13 (61.9)	8 (38.1)	21		
	51–60	4 (26.7)	11 (73.3)	15		
	> 60	0 (0.0)	4 (100.0)	4		
Education	Primary	2 (66.7)	1 (33.3)	3	20.034	0.001
	Secondary	19 (73.1)	7 (26.9)	26		
	Tertiary	66 (80.5)	16 (19.5)	82		
	None	1 (11.1)	8 (88.9)	9		
Residence	Rural	26 (53.1)	23 (46.9)	49	17.404	0.001
	Urban	62 (87.3)	9 (12.7)	71		
Gender	Male	32 (62.7)	19 (37.3)	51	5.085	0.024
	Female	56 (81.2)	13 (18.8)	69		
Total		88 (73.3)	32 (26.7)	120		

and 20.8% for significant fibrosis and cirrhosis, respectively, by Ndububa et al¹² in their study carried out in the western part of Nigeria among symptomatic patients. Likewise, Feng et al¹⁶ and Zhang et al¹⁷ also reported significantly higher values, 65.5% and 75.5%, respectively, for significant fibrosis from their studies among the Chinese population. The inclusion of those with symptoms and features of liver decompensation in their studies could account for the low values of both significant liver fibrosis and cirrhosis from this study compared to the above ones with higher prevalence. Because patients with symptoms of hepatic decompensation are expected to have a higher degree of significant fibrosis and cirrhosis compared to asymptomatic ones.

This study also revealed the positive relationship between the degree of fibrosis and age. It further establishes that the degree of liver fibrosis increases with an increase in age among those with CHB (with a linear regression coefficient (r) of 0.347 and $P < 0.001$). This is similar to other previous reports of increased susceptibility to liver fibrosis with increasing age.¹⁸⁻²⁰ This has been attributed to longer duration of exposure to the virus, coupled with a decline in the regeneration capacity of the liver with an increase in age.¹⁸⁻²⁰

There were statistically significant associations between significant liver fibrosis and the following factors: age group, gender, educational level, and residence. These findings suggest that demographic and socioeconomic factors play a substantial role in the burden of liver fibrosis within the studied population. Previous studies have also recorded a significant association between age, gender, and liver fibrosis, with a higher prevalence in males and the older age group.^{19,21} These findings have been largely attributed to the inhibition of fibrinogenesis by oestrogen in females, which slows down the development and progression of fibrosis.^{19,20}

Additionally, the higher prevalence in the older age group has been linked to the liver's diminished capacity to regenerate with prolonged exposure to the aetiology of fibrosis as age advances.^{19,21} While some studies link low educational level to increased liver fibrosis^{22,23}, others report no significant association.²⁴ Similarly, studies on residential areas show mixed findings;²⁴⁻²⁶ some report higher fibrosis rates in rural populations^{25,26}, while others find no difference between rural and urban dwellers.²⁴

CONCLUSION AND RECOMMENDATION

The prevalence of significant fibrosis of 26.7% among asymptomatic CHBV patients puts them at risk of progressing to HCC or developing other complications related to liver fibrosis. Hence, the need for every HBV patient to have a liver fibrosis assessment done as early as possible after HBV diagnosis.

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