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Original Article

Duplex Doppler Assessment of Portal Vein Congestive Index in Asymptomatic Hepatitis B Virus infected Patients in a Resource Limited Set-up: A Case-Control Study

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Abstract

Background: *A good number of patients with viral hepatitis are asymptomatic and detected as incidental findings. Early detection of the hemodynamic changes as well as prompt treatment is paramount to prevent the development of complications such as portal hypertension, liver cirrhosis and hepatocellular carcinoma. The congestive index (CI) of the portal vein has a high sensitivity and specificity in the diagnosis of hepatic fibrosis and portal hypertension and it is therefore imperative to assess these categories of patients using this index. The objective of this study is to compare the portal vein CI of patients with asymptomatic hepatitis B viral infection and normal individuals"*

Methods and Patients : *This is an institution-based case-control study comprising 112 cases with serological diagnosis of hepatitis B viral infection and 112 age and sex-matched controls that were seronegative for hepatitis B and C viral infection and had normal LFT parameters. The CI of the participants were obtained using duplex Doppler ultrasound, and the data obtained were analyzed using statistical package for social sciences (IBM SPSS version 23.0. Armonk, NY).*

Result: *224 participants made of 112 cases and 112 age and sex-matched controls were evaluated. The age of the participants ranged from 18-63 years. 113 (50.4%) of the participants were males, while 111 (49.6%) were females. The mean value of the portal vein CI was 0.04±0.003cmS among controls and 0.06±0.01cmS among cases; however, the difference was not statistically significant (p 0.192). CI was noted to increase with age and was higher among the male gender, but the difference was also not significant statistically. Also, LFT parameters among the participants was higher in cases than the control and most were statistically significant except for ALP and AST.*

Conclusion: *The CI of the portal vein and LFT parameters were higher in cases than control and and it may therefore be a useful tool in the assessment of patients with hepatitis, particularly in symptomatic cases.*

Keywords: *Portal vein, congestive index, asymptomatic hepatitis B virus patient*

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Introduction

Infection with hepatitis B is a serious health challenge to the general public. About 2 billion people worldwide have hepatitis B viral infection and 350 to 400 million have chronic hepatitis B viral infection with about 620,000 dying annually.[1] Hepatitis B viral infection is endemic in many continents including Africa, and Nigeria has a very high prevalence of 12.2%.(2,3)

Most patients with viral hepatitis are asymptomatic and can present this way for years and even decades. The presentation could be mild and may not cause significant liver disease, but in some patients, there could be continued inflammation which can lead to fibrosis, hepatic steatosis, cirrhosis, liver failure and liver cancer.[4] It is an established fact that progression of liver disease is accompanied by histological changes of the hepatic parenchyma such as hemodynamic changes, inflammation, necrosis, and fibrosis.(4,5)

Hepatitis B surface antigen (HBsAg) is the investigation of choice for screening for HBV infection. (6) Although about 15% to 40% of hepatitis B virus carriers will develop hepatic complications such as cirrhosis, hepatic decompensation and hepatocellular carcinoma, most patients will remain asymptomatic.(7) The vascular complication that could arise from chronic viral hepati-

tis include portal hypertension with or without porto-systemic shunts, flow changes in the hepatic artery and vein, thrombosis of the portal vein, and neovascularization of liver tumour. (8) The severity of the changes involving the hepatic vasculature depends on the degree of fibrosis progression. (9)

Evaluation for liver fibrosis is essential in monitoring patients with asymptomatic chronic hepatitis B viral infection, to assess the progression of liver disease, and this determines when to institute drug therapy. Liver biopsy is still considered the gold standard, but it is an invasive procedure associated with risks and mis-classifications which is not well accepted by patients, making it unsuitable for regular follow-up examinations. This has over the years led to investigations with non-invasive modalities such as transient elastography and portal vein congestive index. (8,9) Transient elastography is particularly preferred to liver biopsy for diagnosis and follow-up examinations of fibrosis but more hands-on training and availability of the needed software will be necessary to make it more effective in our setting.

Grey-scale ultrasonography of the liver may provide important findings related to parenchymal changes in patients with viral hepatitis especially when complications arise but it cannot assess hemodynamic changes hence, the need for Doppler assessment.(10) Due to the limitations associated with the different values from many Doppler parameters of the liver vasculature, researchers have used some new indices for more reliable evaluations such as portal vein congestion index, modified hepatic index (MHI), arterioportal ratio and portal hypertension ratio.(10)

Various parameters have been used to evaluate the portal vein including diameter, cross sectional area, pulsatility index, mean flow velocity and congestive index but the latter is the most reliable, sensitive and specific parameter.(9,11-15) Assessing patients with this index will go a long way in averting the sequalae associated with viral hepatitis in our environment hence, the motivation for this study.

Methods

This prospective case-control study was carried out in the Radiology Department of University of Abuja Teaching Hospital following ethical approval by the Research and ethics committee of the institution. A total of 224 participants within the ages of 18 – 63 years made up of 112 cases and 112 controls were recruited. The cases were consenting asymptomatic adult patients with serological diagnosis of hepatitis B viral infection who met the inclusion criteria and referred to the Radiology Department for abdominal ultrasound scan from Internal Medicine and Family Medicine departments of the institution. The controls were consenting staff and students as well as eligible patients on medical check-up from the Family Medicine Department. The liver function test parameters of this category of patients were normal and they were also seronegative for both hepatitis B and C virus infections. Those excluded from the study were patients with obesity, renal diseases, liver diseases from other causes other than hepatitis. Pregnant women and lactating women as well as patients under 18 years of age were excluded from the study.

After obtaining an informed consent, the biodata and relevant clinical history were obtained to establish inclusion and exclusion criteria. Anthropometric measurements (height and weight) were obtained and BMI was then calculated using the formula Body Mass Index (BMI) = weight (kg)/height^2 (m^2). (16) About 5 milliliters (mls) of venous blood was then taken from all participants and the samples were evaluated at the Microbiology and Chemical Pathology Departments respectively for Hepatitis B and C screening using rapid test strips, and spectrophotometric assay for LFT parameters (bilirubin, total protein, albumin, liver enzymes [alkaline phosphatase, alanine transaminase and aspartate transaminase]). After ascertaining the eligibility of the participants, they were scanned with low frequency curvilinear probe (2.5MHz to 5.0MHz) on the Logic F8 expert GE (General Electric, USA 2016) colour Doppler ultrasound machine.

Following an overnight fast, the patients were asked to lie supine on the ultrasound couch, ultrasound coupling gel was applied on the abdomen and B mode grey-scale 2D ultrasound scan of the abdomen was performed. Using the right subcostal/intercostal approach, the entire liver was scanned in longitudinal, transverse and oblique planes, and the following parameters were evaluated: liver span, gall bladder wall thickness, longitudinal and transverse dimension of the gallbladder and the splenic length. The peritoneal cavity was also assessed for possibility of ascites.

The portal veins parameters (diameter, cross sectional area, mean flow velocity and then congestive index) were also evaluated at the level of the porta hepatis as shown in figures 1 and 2 below. The Doppler interrogation was done with Doppler angle of 60^0 with a sample size of 4mm-8mm. The mean flow velocity was calculated using $0.57Vmax/Cos\theta$.[9] The θ in this case was the Doppler angle 60^0 while the 0.57 was the correction factor of parabolic flow. Congestive index of the portal vein was then calculated by dividing the cross-sectional area by the mean portal vein flow velocity. All measurements were obtained twice and the average calculated to eliminate intra-observer variability

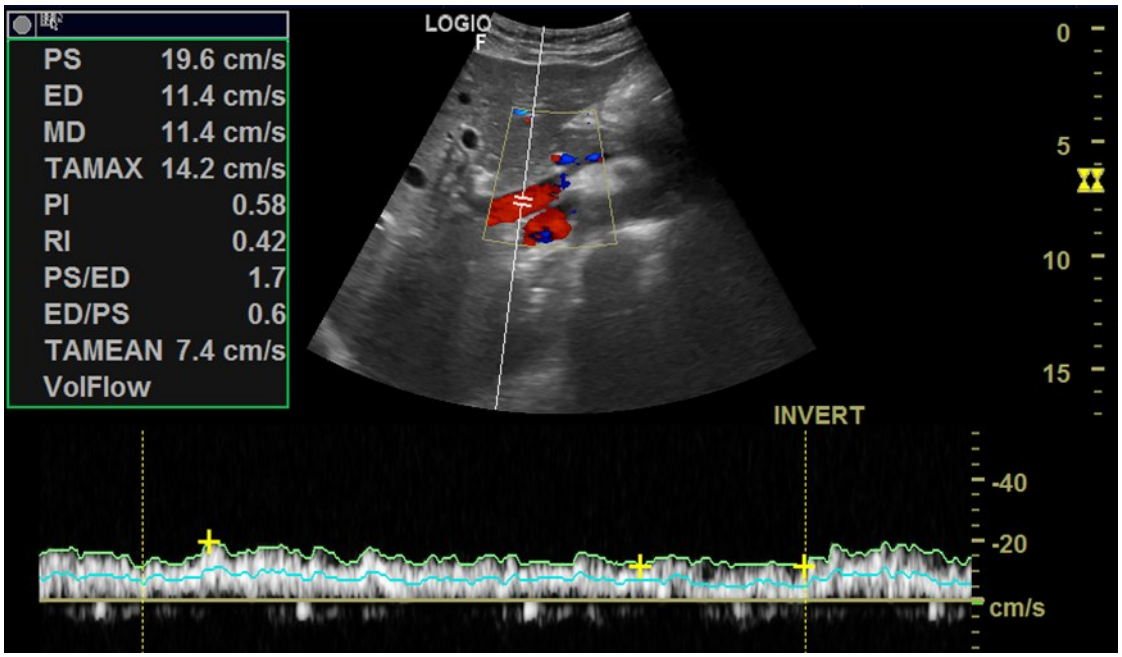

Figure 1: B -mode Ultrasound of the portal vein in transverse plane showing the cross-sectional area of the portal vein at the porta hepatis (1.01cm^2).

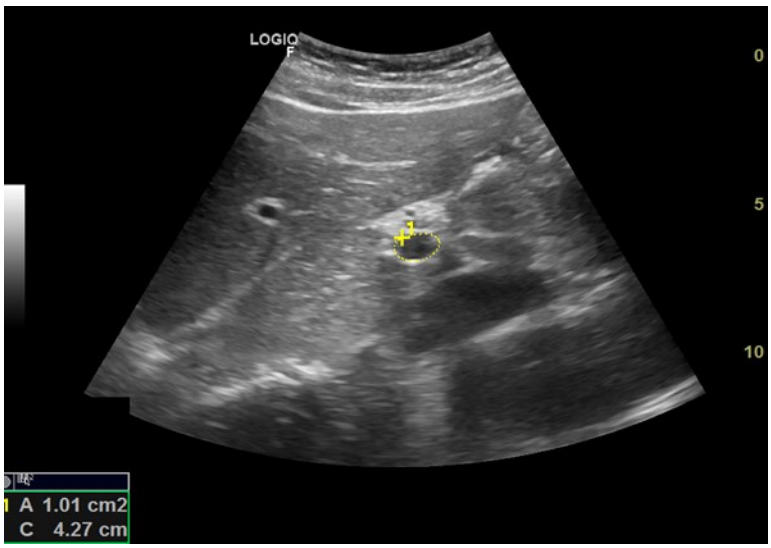

Figure 2: A duplex Doppler ultrasound scan of the portal vein at the porta hepatis demonstrating the normal spectral waveform of the portal vein (monophasic forward flow (hepatopetal) with mild respiratory phasicity and cardiac periodicity

Ethical considerations
Ethical approval was obtained from the Research Ethical Committee of the Hospital (No. UATH/HREC/PR/2018/012). The patients were provided with adequate counselling and care as appropriate and informed consent was obtained before their inclusion in the study.

Results
Data obtained from the 224 adult participants was analyzed with SPSS version 2021. Out of the study participants, 113 (50.4%) were males, while 111(49.6%) were females, with Male to Female ratio of approximately 1:1. This was comprised of 53(47.3%) males and 59(52.7%) females among the controls while 60(53.6%) males and 52(46.4%) females were in the case group as shown in Table 1. There was no statistically significant difference between gender (P = 0.350). The age of participants ranged from 18 to 63 years. The mean age for the controls was 36.47years ±10.72 years, while that of the cases was 36.75years ±9.78 years; and there was no statistically significant difference between the ages of the two groups (p-value 0.350). 34.8% of the controls and 37.5% of the cases were between 30-39 years of age, making it the largest age group in this study.

Table 1: Socio-demographic characteristics of respondents

Variables	Control (n=112)	Case (n=112)	χ^2/FET	p-value
Age (Mean±SD)	36.47±10.72	36.75±9.78	-0.202(t-test)	0.840
Gender				
Male	53(47.3)	60(53.6)	0.875	0.350
Female	59(52.7)	52(46.4)		
Total	112(100.0)	112(100.0)		
Age				
<20 years	3(2.7)	0(0)	3.434**	0.657
20-29 years	30(26.8)	28(25.0)		
30-39 years	39(34.8)	42(37.5)		
40-49 years	24(21.4)	28(25.0)		
50-59 years	13(11.6)	12(10.7)		
60-69 years	3(2.7)	2(1.8)		
Total	112(100.0)	112(100.0)		
Level of education				
None	1(0.9)	0(0)	5.029	0.136
Primary	2(1.8)	3(2.7)		
Secondary	10(8.9)	20(17.9)		
Tertiary	99(88.4)	89(79.5)		
Total	112(100.0)	112(100.0)		

*p-value significant at <0.05
** FET = Fisher's exact test

The mean weight among the control was 67.11kg ±8.34, while that among the cases was 67.45kg ±9.33 and there was no statistically significant difference between the two groups (p 0.774) as shown in Table 2.

There was a statistically significant difference between the BMI of the participants in the control and case groups (P 0.041) as shown in Table 2.

Table 2: Anthropometric distribution of respondents

Variables	Control Mean±SD	Case Mean±SD	t-test	p-value
Weight (Kg)	67.11±8.34	67.45±9.33	-0.287	0.774
Height (m)	1.65±0.07	1.69±0.09	-2.991	0.003*
BMI (Kg/m^2)	24.48±2.71	23.72±2.88	2.054	0.041*

**p-value significant at <0.05*

The liver function test parameters (Total Bilirubin, Direct Bilirubin, ALAT, Total Protein and Albumin) were found to be statistically different across the cases and control except for the ALP and AST of which showed no statistically significant difference as depicted in table 3. The mean value of Total Bilirubin and Direct Bilirubin were higher in cases than controls with a P value of 0.002 and <0.001 respectively. ALAT and Total Albumin were also higher in cases than control with a P value of 0.009 and 0.002 respectively.

Table 3: Comparison of Liver Function Tests among cases and controls

Variables	Control Mean±SD	Case Mean±SD	t-test	p-value
Total bilirubin	12.32±4.36	14.48±5.81	-3.153	0.002*
Direct bilirubin	4.86±2.33	6.20±3.08	-3.670	<0.001*
ALP	178.96±50.38	176.15±41.97	0.454	0.650
ASAT	23.73±12.11	25.21±10.15	-0.987	0.325
ALAT	22.93±9.94	27.34±14.58	-2.648	0.009*
Total protein	75.68±3.83	77.65±5.46	-3.128	0.002*
Albumin	44.25±3.47	46.16±4.19	-3.718	<0.001*

*p-value significant at <0.05

The grey-scale ultrasound findings and measurements of the liver, gallbladder and spleen of the participants were all obtained. The mean liver span was 14.58cm±1.39 and 14.24cm ±1.38 among controls and cases respectively. There was no statistically significant difference between the value of the liver span, gallbladder length, gallbladder breadth, gallbladder wall thickness and spleen size for the two groups, and the parenchymal echopattern of these organs in both groups was within limits of normal. The mean values for the portal vein cross-sectional area (PVCSA), mean flow velocity (MFV) and portal vein congestive index (PVCI) among control and case groups are as shown in Table 4. The aforementioned portal vein indices were found not to be significantly different across cases and controls.

The portal vein congestive index (PVCI) was higher among the cases with a mean value of 0.06 ±0.01cms as against controls with a mean of 0.04 ±0.026cmS. However, this was not statistically significant (p = 0.192). This is depicted Table 4. The PVCI among cases ranged between 0.010 to 1.100cms with a mean value of 0.056cmS ±0.01 while that among controls ranged between 0.010cmS to 0.0470cmS with a mean value of 0.040cmS.

Table 4: Comparison of sonographic findings of portal vein indices among cases and controls

Variables	Control Mean±SD	Case Mean±SD	t-test	p-value
PVCI	0.04±0.03	0.06±0.01	-1.311	0.192
VMAX	28.09±5.59	28.77±6.91	-0.812	0.418

**p-value significant at <0.05*

Association between PVCI and age among cases showed an increase in PVCI with increasing age as shown in Table 5. Also.,PVCI was higher in males than females (0.07cmS± 0.015 and 0.04cmS±0.006 respectively), but the differences that existed between them was not statistically significant (p = 0.292). The correlation analysis between PVCI and LFT parameters demonstrated weak positive correlations that were not statistically significant except for albumin which showed a weak negative correlation with no statistical significance

Table 5: Comparison of PVCI with age among cases using ANOVA

Variables	N	PVCI Mean±SD	F-value	p-value
Age grouping				
≤20 years	3	0.035±0.002	1.104	0.351
21-40 years	76	0.044±0.050		
41-60 years	32	0.087±0.199		
61-80 years	1	0.033		
Total	112	0.056±0.115		

*p-value significant at ≤ 0.05
**F = ANOVA value

Discussion

A total of 224 participants were included in the study, which comprised 112 cases and 112 controls that were age and sex-matched. The age of the participants ranged from 18 to 63 years with a mean age of 36.8±9.8 and 36.5 years ±10.7 among cases and controls respectively. The mean age among the cases is similar to that of the previous study carried out by Onyekwere and co-workers, (17) where the mean age of cases found to be seropositive for hepatitis B virus following a screening exercise was 36.1 ± 8.8 years. This shows that youths are more affected as Hepatitis is largely sexually transmitted and youths are more sexually active. Among the cases, there were more males 60(53.6%) than females 52(46.4%) which is also in agreement with the studies of Onyekwere and Baig where the prevalence of hepatitis B virus infection was found to be more in males. (17,18)

PVCI across age-groups among the cases showed an increase with increasing age as that connotes chronicity and possibly severity of the disease. Aiyekomogbon and co-researchers also demonstrated an increase in congestive index with increasing age in their study. (19) As the congestive index of the portal vein was higher in cases than controls, so also the values of all the liver function test parameters were higher in the cases when compared with the controls. These observations suggest that laboratory evaluation of liver function test and Doppler assessment of portal venous flow are sensitive in monitoring patients with asymptomatic hepatitis B virus infection who have normal clinical and grey-scale hepatic ultrasound scan findings. Congestive index of the portal vein is therefore a strong diagnostic parameter for early detection of subtle hepatic changes in patients with hepatobiliary disease. To the researchers' knowledge, correlation of PV congestive index with liver function test has not been studied previously in our immediate environment. A study done in Italy however established a strong positive correlation between alanine aminotransferase levels and transient elastography by Fibroscan in the evaluation of liver stiffness in hepatitis B virus carriers (t= 4.740, p-value <0.001), the alanine aminotransferase showed progressive decrease during antiviral therapy which paralleled the findings using transient elastography with Fibroscan.(20) This suggests that evaluation of the portal vein congestive index and correlation of its findings with those of liver function test may be beneficial in monitoring patients with hepatitis B virus infection.

recorded in the studies of other authors in Japan and Nigeria where they had respective mean values of 0.070cmS ±0.029 and 0.0722cmS ±0.0135. (9,19) The differences could be attributed to the inter-equipment and inter-observer variability. (21,22) Based on our observation, the congestive index of the portal veins for both groups were within limits of normal but those with viral hepatitis was higher than the control group. The normalcy recorded in the case group is anchored on the fact that asymptomatic hepatitis patients were considered and the higher value recorded for hepatitis patients as against the control in this study gives credence to the sensitivity of congestive index in the assessment of liver diseases and fibrosis. Subtle fibrotic changes may have taken place despite the fact that they were asymptomatic, bearing in mind that liver has high residual capacity. There was an increase in the mean value of the congestive index among the cases when compared with the control which is similar to the observation of other authors in Japan and India.(9.21) The difference found in the index study was however not statistically significant as the study was exclusively carried out among asymptomatic patients (P = 0.192). A previous study by Sato and co-researchers (23) revealed the mean values of congestive index as 0.007±0.028cmS in patients with chronic inactive hepatitis and 0.09±0.05cmS in patients with chronic active hepatitis and results obtained suggested that the congestive index which is a measure of the portal venous pressure and hepatic fibrosis began to increase at the stage of chronic active hepatitis. This study recruited only asymptomatic cases, thus unable to corroborate this PVCI finding in patients with advanced liver disease.

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Authors' Contribution

HM: Actively participated in the sonographic assessment of the patients and she also contributed substantially to the conception, design and writing of the manuscript

J.O.A: Contributed substantially to the conception, design and writing of the manuscript, and he is the corresponding author of the article.

U.D.I: made substantial input to the writing of the manuscript. She also reviewed and corrected the entire article before submission.

O.O.O: made substantial input to the writing of the manuscript. She also reviewed and corrected the entire article before submission.

K.H.O: Contributed substantially to the design and writing of the manuscript.

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