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Prevalence and Determinants of Hepatic Steatosis in Chronic Hepatitis B Virus Infection

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ABSTRACT

Background and aim: Globally, viral hepatitis B and C are the leading causes of chronic liver disease. Viral hepatitis is highly prevalent in Sub-Saharan Africa with a 5-20% carrier rate in the general population and a high mortality of up to 10.8/100,000 in some regions. Patients with chronic Hepatitis B (CHB) are also affected by lifestyle related challenges of obesity, alcoholic liver disease, metabolic associated fatty liver disease affecting the larger populace thus we set out to determine the prevalence and risk factors for hepatic steatosis in CHB patients.

Methodology: This was a cross-sectional retrospective study of 114 CHB patients. All study participants were screened for baseline parameter and abdominal sonography was performed by an expert radiologist to detect the presence of hepatic steatosis.

CHB patients attending the Gastroenterology outpatient clinic of the Rivers State University Teaching Hospital (RSUTH) between November 2022-April 2023 were included in the study.

Data was collected through review of hepatitis B register and patients' interview. Data was analyzed using the statistical software package SPSS version 22. Bivariate logistic regression analysis was used to identify variables influencing Hepatic steatosis and p-values <0.05 were considered statistically significant. Hepatic steatosis was defined as fat accumulation of >5% in the hepatocytes on abdominal ultrasound scan.

Results: The prevalence of Hepatic steatosis was 29.8% and BMI, older age, raised blood glucose (r=0.553, *p*=0.000, r=0.295 *p*=0.026, r=0.457 *p*=0.000 respectively), including HBeAg negativity ($\chi 2$=15.774, p=0.000) were significant determinants of its occurrence. There was no significant relationship between HBV DNA levels and Hepatic steatosis.

Conclusion: Hepatic steatosis is common in CHB patients and both metabolic and virological factors play a role in its occurrence.

Abbreviations: chronic Hepatitis B(CHB), HBV DNA (Hepatitis B virus DNA).

INTRODUCTION

Fatty liver or hepatic steatosis is the accumulation of triglycerides in the hepatocytes which occurs when intrahepatic fat is greater than or equal 5% of Liver weight. (1)

Hepatitis B(HBV) is a global health challenge which affects over 2 billion people and results in over 600,000 annual deaths. (2)

Globally, viral hepatitis B and C are leading causes of chronic liver disease(3) though there has been a predictable decline in recent years due to the availability of 'cure' for hepatitis C, and an increased global preventative strategy for HBV. Furthermore, the availability of newer and better treatment options, well placed control and preventative measures has resulted in a decline in CLD- related age adjusted mortalities from 21 deaths/100,000 persons to 16 deaths/100,000 persons from 1990-2017. (4)

Chronic hepatitis B (CHB) infection is highly prevalent in Sub-Saharan Africa with a 5-20% carrier rate in the general population and a high mortality of up to 10.8/100,000 in some regions.(5) Lazano et al (6) reported an increasing trend in cirrhosis related mortality of up to 31% within a 20 year period (1990-2010) with viral hepatitis related cirrhosis as a major etiology. Arguably, chronic viral hepatitis related cirrhosis and Hepatocellular carcinoma could rank among the top ten causes of mortality worldwide. (7)

In a 2017 report from 193 countries by the global, regional and national collaboration on the burden of cirrhosis(8), hepatitis B was reported to account for 31.5% and 24% of cirrhosis-related deaths in men and women respectively. In the same report, hepatic steatosis was reported as the cause of death in 7.7% and 11.3% of men and women respectively. (8)

Patients with CHB are also affected by lifestyle related challenges of obesity, alcoholic liver disease (ALD), Metabolic associated liver disease (MALD) or Non-alcoholic fatty liver disease (NAFLD) affecting the larger populace. Thus, there is a global trend towards increased alcohol consumption (9) accounting for 30-50% of cirrhosis related death (10,11) and a disproportionate chronic liver disease and cirrhosis-related mortality in young people less than 45years of age (12,13) which is the same age bracket most affected by CHB- related liver diseases in Sub-Saharan Africa. (14)

With the increasing burden of alcohol and metabolic fatty liver disease in Africa owing to the adoption of western lifestyle, obesity, diabetes mellitus, HIV and much more added to the already existing high prevalence and incidence of viral hepatitis occasioned by poor screening, inadequate disease surveillance and poor access to healthcare, CHB- related liver diseases especially NAFLD may soon be a major cause of morbidity and mortality in Africa identical to that of HIV and malaria.

METHODOLOGY

Study site and Participants: This was a cross-sectional study of 114 chronic viral hepatitis B patients attending the Gastroenterology outpatient clinic of the Rivers State University Teaching Hospital (RSUTH) in southern Nigeria between November 2022-April 2023. Data was collected through review of hepatitis B register and patients' interview. Ethical approval was obtained from the hospital ethical committee with approval number RSUTH/REC/2022213.

Inclusion criteria: eligible adult patients who are 18years and above with HbeAg positivity for > 6months who gave an informed consent were included in the study.

Exclusion criteria: Patients <18years of age, with a self-reported history of significant alcohol consumption >14 units/day and/or pregnant females were excluded. Also, patients who are known diabetic, and those who are positive for HCV antibody and/or HIV were excluded from the study.

Materials and method: All study participants were screened for baseline parameters including HCV-Ab, HIV, Fasting blood sugar (FBS), total cholesterol (CHOL), low density cholesterol (LDL), high density cholesterol (HDL), triglyceride (TG), ammonium aminotransferase (ALT) and aspartate aminotransferase (AST) were measured with enzymatic photometry on blood samples. Height and weight were evaluated and Body mass index (BMI) was calculated with weight (in kilograms) over height squared (in meters). Persons with BMI 18.5 to 24.9 was considered normal Persons, with BMI of more than 25-29.99 were considered overweight, and more than 30 obese.

Abdominal sonography was performed by an expert radiologist to detect the presence of hepatic steatosis. Hepatic steatosis which is fat accumulation of >5% in the hepatocytes was graded into mild, moderate and severe (15): -

Mild Hepatic steatosis: diagnosed when there was raised hepatic echogenicity in contrast to the kidney cortex.

Moderate Hepatic steatosis: in addition to raised echogenicity there is blurring of the vessels.

Severe Hepatic steatosis: Severe form of fatty liver was diagnosed based on disappearance of diaphragm in addition to the features of the mild and moderate form.

Data was analyzed using the statistical software package SPSS version 22. Bivariate logistic regression analysis was used to identify variables influencing

Hepatic steatosis and p-values <0.05 were considered statistically significant.

RESULTS

Socio-Demography of the Study Population

This was a cross-sectional study of 114 chronic hepatitis B infected patients with a mean age of 36.04 ± 7.238years (range 18-44years). (figures 1 & 2). Chronic HBV patients with a significant history of alcohol consumption were excluded from the study.

There was a predominance of males in the study population compared to females (68, 59.6%**:** 46, 40.4%), and a larger proportion of the study population were civil servants and unemployed persons (38[33.3%], 14[12.3%]). figure 3. The study participants were fairly educated (table 1) with a strong urban residency (112, 91.2%).

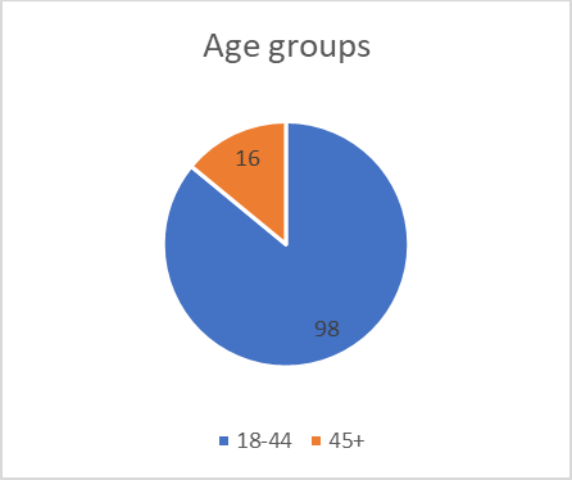

Figure 1: age distribution of the study population.

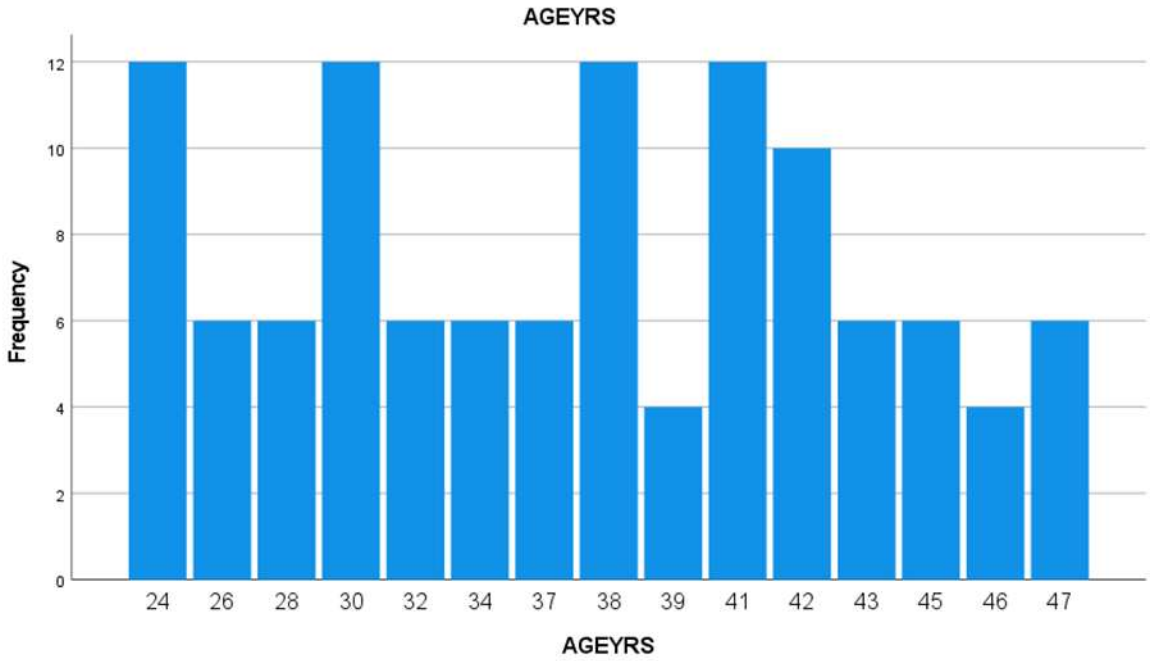

Figure 2: bar chart of the age distribution of the study population.

Table 1: Educational level of the patients

EDUCATION LEVEL	N	%
Primary	0	0%
Secondary	62	54.4%
Tertiary	52	45.6%

Table 2: Residency of the patients

RESIDENCE	N	%
Rural	10	8.8%
Urban	112	91.2%

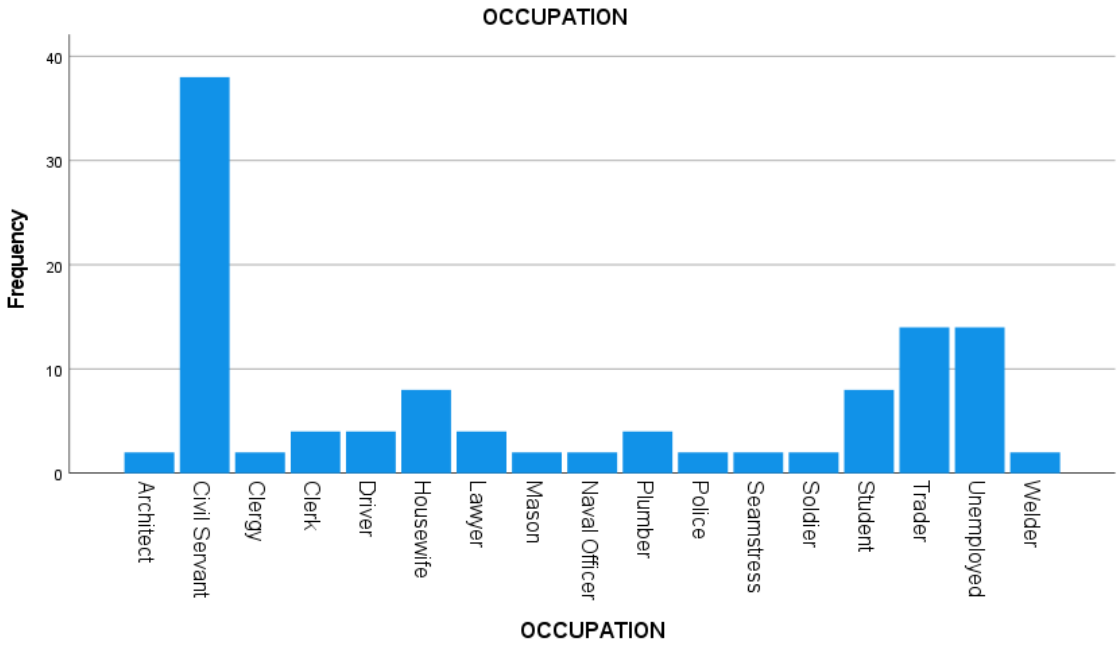

Figure 3: distribution of occupation among the study population

PREVALENCE OF HEPATIC STEATOSIS AND ITS DETERMINANTS

Hepatic steatosis was found in 34 of the 114 patients giving a prevalence of 29.8% (Figure 4). The presence of Hepatic steatosis sonographically significantly correlated with age (r=0.295, *p*=0.026), raised BMI (r=0.553, *p*< 0.001), elevated fasting blood glucose (r=0.457, *p*<0.001), and high ALT levels (r=0.292, *p*=0.002). No significant relationship was found between steatosis and initial HBV load nor duration of HBV diagnosis in years. (r = 0.052, *p* = 0.580 r = -0.088, p = 0.354 respectively). However, male patients and HbeAg negative chronic HBV patients were most likely to develop Hepatic steatosis ($\chi 2$ = 5.696, *p* = 0.017) (X^2 = 15.774, *p*<0.001).

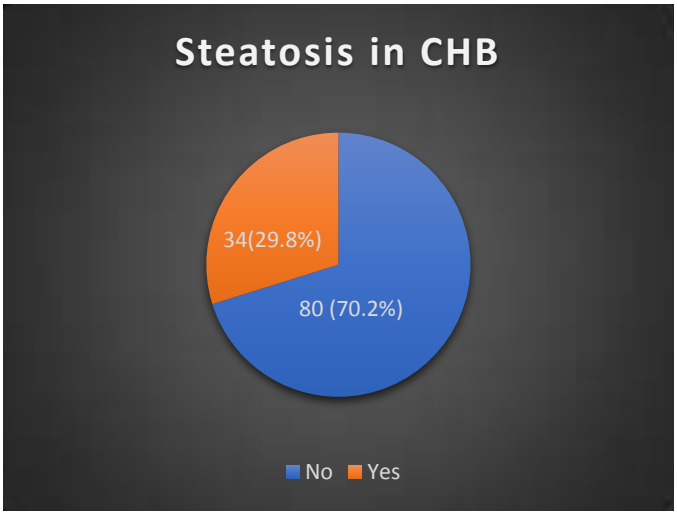

Figure 4: prevalence of Hepatic steatosis

Table 3: Association of risk factors with Hepatic steatosis

Determinant	R- value	*P*-value
Age	**0.295**	**0.026**
BMI	**0.553**	**0.001**
Fasting blood glucose	**0.457**	**0.001**
ALT	**0.292**	**0.002**
AST	**0.148**	**0.117**
Initial Viral load	**0.088**	**0.354**
HBV duration (years)	**0.052**	**0.58**

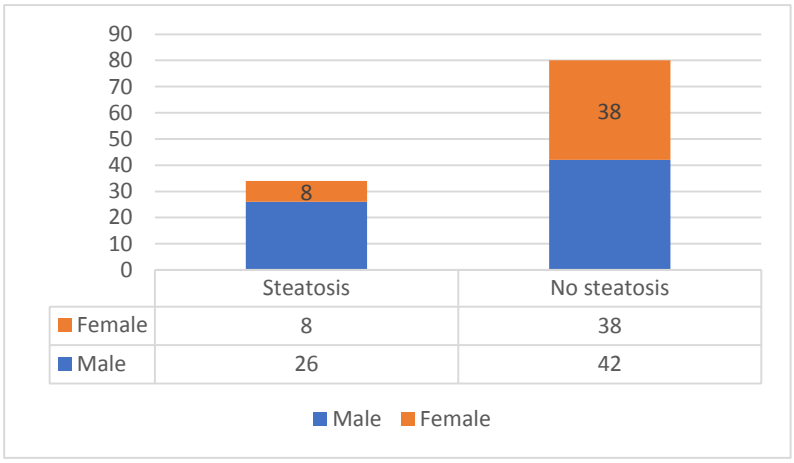

Figure 5: relationship of Hepatic steatosis to sex

Significant relationship between sex and steatosis $\chi^2 = 5.696$, $p = 0.017$

PRESENTING COMPLAINTS AT FIRST VISIT

There were varied presenting complaints by the participants at their first presentation to the clinic as shown in table 4, the most common of which was fatigue (18.2%). Others were abdominal swelling (10.2%), early satiety (3.4%), abdominal pain (3.4%), and leg swelling (4.5%). Notably, non-gastrointestinal related complaints comprised a significant proportion (19.3%) of patients' complaints at first visit. Furthermore, 2.3% of our study population was diagnosed of hepatitis B during compulsory pre-employment screening.

Table 4: frequency of presenting complaint of the study population

Complaint	Frequency	Percentage
None	64	36.4
Early Satiety	6	3.4
Fatigue	32	18.2
Abdominal Pain	6	3.4
Abdominal Swelling	18	10.2
Anorexia	4	2.3
Leg Swelling	8	4.5
Others	34	19.3
Pre-Employment	4	2.3
Total	**176**	

DISCUSSION

This retrospective study of 114 chronic HBV patients sought to examine the association between Hepatic steatosis and possible risk factors in a Nigerian cohort.

Globally, studies on Hepatic steatosis, especially on the NAFLD/MAFLD subset has gained preeminence in recent years including studies on Hepatic steatosis in viral hepatitis B. There is however a dearth of information on the burden and spectrum of NAFLD in African populations, both from population-based and clinical studies (16). The paltry clinic- based studies available are mostly in Type 2 Diabetes mellitus and HIV and the reported prevalence of sonographically detected NAFLD in Nigeria varies from 9.5% to 68.8%.(17–20) Our reported prevalence of 29.8% is also in consonance with these reported figures and is similar to the prevalence trends obtained in Asia (21) and the western world. (22)

Our observation of a higher number of males with Hepatic steatosis compared with females ($\chi 2 = 5.696$, $p = 0.017$) is similar to a finding in a South African study that reported a lower Hepatic fat content in African women. (23)

Consistent with findings from other studies (24,25), we observed that older age($r = 0.295$, $p = 0.026$) and hyperglycemia ($r = 0.457$, $p < 0.001$) were significantly associated with the incident of Hepatic steatosis. Also in accordant with other studies (26–28), our study showed that there is an increased risk for Hepatic steatosis in patients with raised ALT levels ($r = 0.292$, $p = 0.002$). Moreover, our finding that obesity is an independent risk factor for Hepatic steatosis in chronic HBV subjects ($r = 0.553$, $p < 0.001$) was consistent with other studies and is similar with the general population. (29,30)

The spectra of presenting complaints of the patients in our study (table 4) divulge that most of our patients present late when symptoms of Liver disease have developed. It is a well-known fact that HBV infection is mostly asymptomatic and symptoms only develop when there is some degree of hepatic impairment. This then underlines the exigency for a comprehensive national screening program for viral hepatitis in countries with high endemicity such as Nigeria.

Lastly, in our retrospective cohort, we explored the relationship between viral parameters namely the level of HBV DNA and HbeAg status and the presence of Hepatic steatosis. contradictory to other studies

(31,32) we observed no cogent relationship between HBV DNA viral load and the risk of Hepatic steatosis (r = -0.088, p = 0.354). Our study also demonstrated that the presence of steatosis correlated positively with HbeAg ($\chi 2$ = 15.774, p < 0.001) negativity converse to the finding by Huang et al. (33)

Study limitation: our study is limited by the non-availability of histological data to further stage Hepatic steatosis in our patients as well as the absence of data parameters on factors such as dyslipidemia. Moreover, the retrospective nature of our study is also a limitation and a well-designed prospective study will be needed to thoroughly investigate the interplay between Hepatic steatosis and CHB.

CONCLUSION

In our retrospective study multiple metabolic and virological factors were significant potential determinants of Hepatic steatosis in our cohort including male sex, older age, HbeAg positivity, raised ALT levels, elevated BMI or obesity and hyperglycemia. Concurrent Hepatic steatosis and CHB could potentiate the development of NASH and fibrosis in hepatitis B infected patients.

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Competing interest: the authors declare no conflict of interest.

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