SCREENING INDICATIONS, SOCIO-DEMOGRAPHIC, VIROLOGIC AND RADIOLOGIC CHARACTERISTICS OFVIRAL HEPATITIS B PATIENTS IN A HIGHLY ENDEMIC POPULATION IN SOUTHERN NIGERIA

ABSTRACT

Background

Viral hepatitis B is a life-threatening condition with global public health implications. It is highly endemic and one of the leading causes of mortality in Africa. There are no screening strategies defined for the general population in Nigeria despite an estimated 19 million Nigerians living with Hepatitis B, and a high prevalence of 11-13%.

This study aims to identify indications for Hepatitis B screening, as well as the virologic, radiologic and sociodemographic characteristics of this populace.

Methods

This is a cross-sectional review of the viral hepatitis database of Adult Hepatitis B positive patients. The biodata, laboratory and radiological parameters were analyzed using SPSS version 26 and Categorical variables were reported as frequencies and percentages. Continuous variables were reported as means ±SD, and a p-value of ≤0.05 was considered to be statistically significant.

Results

The mean age of the 454 hepatitis B positive patients was 38.33±11.16years comprising198(43.8%) females and 255(56.2%) males. All six geopolitical regions of Nigeria were represented in the study with the south-south region having the highest representation of 220 patients. Incidental findings such as pre-employment screening, pre-marriage screening, screening before blood donation, pre-surgery screening for non-Hepatic related diagnosis and public health awareness campaigns accounted for 64% of the indications for screening, 4.4% were diagnosed from the compulsory antenatal screening and 11.3% with advanced liver disease.

The majority of patients (94.7%) were HBeAg negative, while HBV DNA levels ranged from <20 to 170,500,000 IU/ml (mean=4,509,723.97 ± 26,264,722.07 IU/ml).

Increased AST and ALT levels were observed in 256 patients (56.4%) and 193 patients (42.5%) respectively.29.7% of the patients had hepatobiliary disease on abdominal ultrasound scan.

Conclusion

This study revealed that Hepatitis B infection in Nigeria cuts across all regions and has a gender disparity with more males affected than females. The majority of the participants were diagnosed incidentally or during an illness, highlighting the importance of routine screening. Additionally, the majority of patients had HBeAg-negative chronic Hepatitis B, indicating the need for effective public health strategies to address this prevalent form of the disease.

Keywords: Hepatitis B, Screening, indications, HBeAg, chronic HBV

Introduction

Viral hepatitis B, a potentially life-threatening and global dilemma with a disparate epidemiology, is a highly endemic infection in Africa affecting approximately 81 million people with viral hepatitis-related liver cirrhosis as one of the leading causes of mortality in Africa.(1,2) The implication of chronic hepatitis B (HBV) infection is progressively being acknowledged with a 2019 WHO report of over 820,000 annual deaths and 1.5million new infections yearly.(1) Furthermore, Lozano et al submitted that HBV now ranks 15th among all causes of human mortality. (3)

Despite the high burden of childhood HBV infection in Africa, horizontal transmission remains the major route of HBV transmission (4) compared with the perinatal route of transmission and in adults, male sex is a major risk factor for chronic HBV infection. (5)

In Sub-Saharan Africa, HBV genotypes E, A and D respectively are the dominant genotypes(6) resulting in a predominance of HBeAg-negative hepatitis B infection. (7) Thus, HBeAg-negative/anti-HBe-positive chronic hepatitis B (CHB) is 7-9 times more common in Africa due to the molecular characteristics of the prevailing HBV genotype. (7)Also, it has been observed that patients infected with subgenotype A1 which is prevalent in Africademonstrate an earlier loss of HBeAg and seroconversion to anti-HBe during the natural course of HBV infection compared to those infected with subgenotype A2. (7)

The 2023 CDC guideline for screening and testing for Hepatitis B virus infection recommends screening for all adults aged 18 years and above at least once in a lifetime using the triple panel test which includes the Hepatitis B surface antigen, antibody to Hepatitis B surface antigen and antibody to core antigen.(8) The CDC also recommends testing for everyone born in regions with HBV infection prevalence of ≥ 2% which includes Nigeria and most Sub-Saharan African countries.(9)A 2021 meta-analysis reported a pooled prevalence of 9.5% for Hepatitis B in Nigeria (10) with the North-Western region having the highest prevalence of 12.1%. this places Nigeria in a region with high endemicity (>8%) for HBV using the WHO criteria. (11)

The Nigerian national guideline for viral Hepatitis in Nigeria (12) published in 2016 recommends routine viral hepatitis screening for high-risk populations such as female sex workers, male sex workers, healthcare workers, and PWID to mention but a few. There, however, were no screening strategies defined for the general population despite an estimated 19million Nigerians living with HBV or HCV, and a high prevalence of 11-13% and 2.1% for HBV and HCV respectively. (13)

Moreover, there are multiple barriers/challenges to screening and access to care for Hepatitis B in Nigeria and these screening challengesinclude inadequate National strategies/ guidelines on viral hepatitis infection in Nigeria especially a lack of screening programs such as the PROLIFICA program in Gambia(14) that will access in-depth level of HBV screening and awareness in both urban and rural centers. Additional challenges comprise Poor funding for Viral Hepatitis program, lack of prioritisationof viral Hepatitis infection by donor agencies in Nigeria, poor

impact of ongoing screening strategies for viral Hepatitis, inadequate supply of test kits, limitation of testing to urban regions of the country, and underdiagnosis of viral Hepatitis due to the use of testing kits that are low in sensitivity and specificity.

Olakunde et al (15) in their study on Barriers to hepatitis B virus screening of pregnant women in primary healthcare centers in Nigeria identified that"perceived barriers exist at patient, provider, and health system levels and they include the lack of test kits, unaffordability of HBV test, shortage of trained personnel, poor awareness and knowledge of HBV, and unavailability of treatment and prevention interventions for HBV."

There are also identifiable barriers to access to treatment currently in Nigeria which may consist of the cost of DNA assays, absence of easy, cheap and noninvasive screening tools for assessment of liver diseases, lack of widespread educational programs on the prevention and treatment of HBV, and restriction of the free generic Tenofovir to HIV-infected patients only thereby discriminating against HBV monoinfected individuals. Furthermore, there is no national access program nor subsidized care for HBV-infected persons and the cost of treatment is borne individually which impacts and impoverishes the patients as reported in a recently published study in southern Nigeria. (16)

Lastly, another noticeable barrier is the HBV knowledge gap among healthcare workers and the general population (15,17) which may affect the demand and uptake of HBV screening test as well as its treatment. This study aims toidentify indications for HBV screening among patients visiting a tertiary outpatient clinic, virologic characteristics as well as the sociodemographic variations of this populace.

Methodology

Rivers State University Teaching Hospital is a 500-bed specialist tertiary health centre with 2 medical schools and residency training programs that serves Rivers State and neighboring states in the south-south region of Nigeria.

This was a cross-sectional,descriptive, observational study conducted by reviewing the database of patients with viral hepatitis B seen from July 2017 to January 2019.

Ethical approval was obtained from the hospital ethical committee with approval number RSUTH/REC/2022213.

Inclusion criteria: Data of Adult HbsAg-positivepatients (>18 years)who remained in treatment for more than 6 months in the outpatient Gastroenterology clinic was obtained from the viral hepatitis B register and included in the study.

Exclusion criteria: Co-infected patients(Hepatitis C and HIV)and patients who have a recent history of vaccination within the past 30 days were excluded from the study.

Classification of the study population

Patients were classified into two main groups according to the initial HBeAg status: HBeAg positive (HBeAg+) and negative (HBeAg-) groups. Radiological assessment was carried out on all patients irrespective of their group as well as laboratory evaluation. The limits of normal /detection were dependent on the laboratory kit available during the study period and were established by our laboratory.

Hepatitis B viral DNA obtained at first visit (initial HBV DNA) also known as Viral load is classified into 3 depending on its levels- undetectable, low and high.

The undetectable level is HBV DNA ≤10iu/ml as determined by the manufacturers of COBAS® TaqMan HBV test (Roche Diagnostics).(18)

Low levelsof HBV DNA were adopted as PCR quantification levels <2000iu/ml and high levelsas HBV DNA ≥ 2000iu/ml. (12)

Data analysis

Data was entered into Microsoft Excel and was exported and analyzed using Statistical Package for Social Sciences (SPSS) version 26. Categorical variables were reported as frequencies and percentages and compared with the Chi-square test. Continuous variables were reported as means ±SD, and the student t-test was used to compare means. A p-value of ≤0.05 was considered to be statistically significant.

Results

Data of Four hundred and fifty-four (454) hepatitis B positive patients with complete data and no contraindication were extracted from the Viral hepatitis registercomprising 198(43.8%) females and 255(56.2%) males. The mean age of the respondents was 38.33±11.16years with a range of 18 to 76 years with a predominance of young people (N=355, 78.2%) Table 1. Notably, over 50% of our study population are in a legally and socially sanctioned union we however did not explore the type of union (table 2).

Table 1: Age distribution of the study population

Age group	Frequency (%)
Young (< X)	355(78.2)
Middle aged (X – Z)	84(18.5)
Elderly (> Z)	15(3.3)

Table 2: marital status of the study population

Marital status	Frequency (%)
Single	124(27.3)
Married	314(69.2)
Divorced	5(1.1)
Widowed	11(2.4)

Geopolitical variation of the study population

Geopolitically, Nigeria consists of 6 regions as shown in Pictograph 1. All regions of the country are represented in the study population showing the cosmopolitan nature of Rivers State as our tertiary Hospital serves the south-south region of Nigeria.

The South-South region being the host, has the highest number at 220 patients while the North-East region has the lowest representation. The distribution of the study population by state is shown in table 3.

Picture 1: Geopolitical distribution of the study population

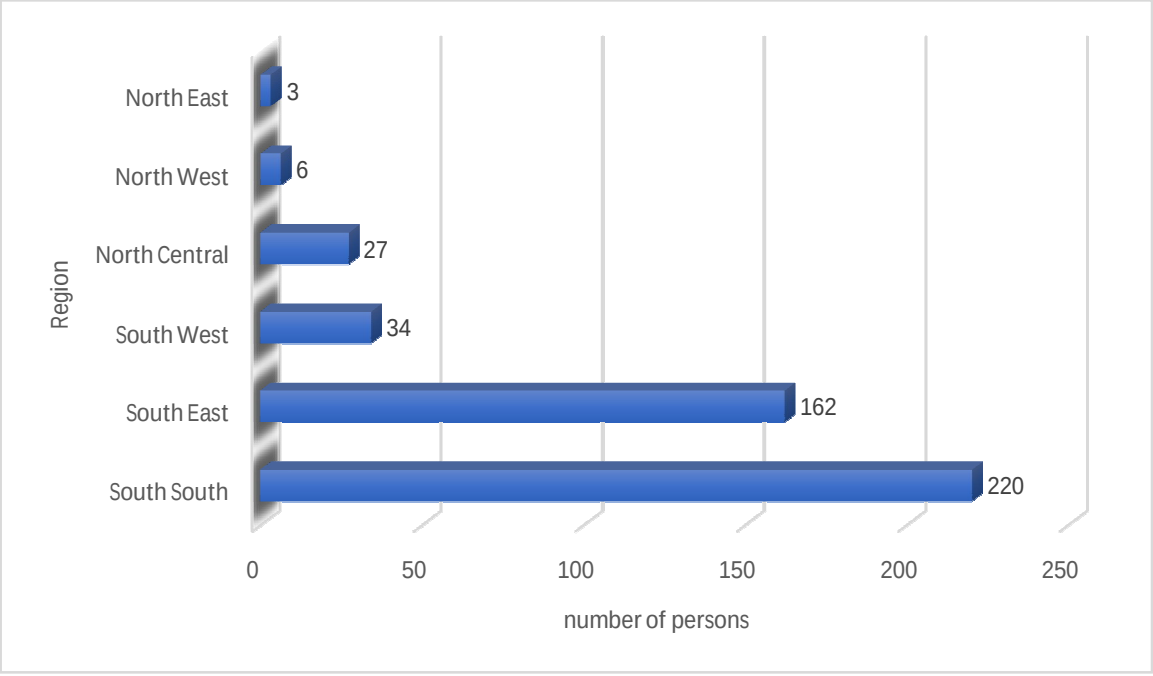
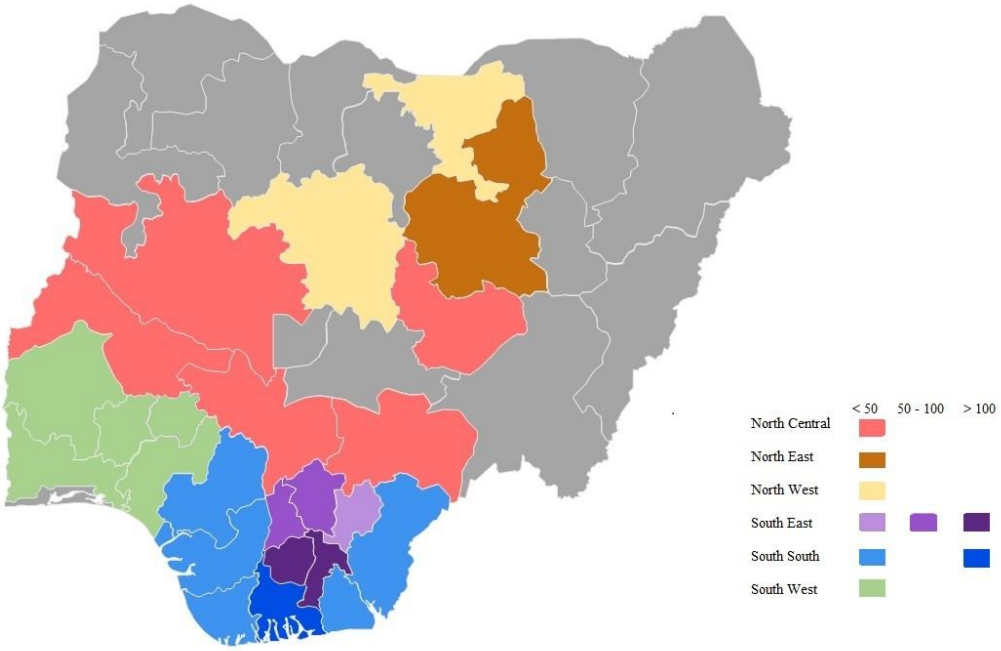


Table 3: Distribution of the study population by State and Nationality

State	Frequency	Percent
Abia	71	15.6
Akwa Ibom	12	2.6
Anambra	14	3.1
Bauchi	3	0.7
Bayelsa	8	1.8
Benue	2	0.4
Cross River	4	0.9
Delta	18	4.0
Ebonyi	4	0.9
Edo	20	4.4
Ekiti	6	1.3
Enugu	12	2.6
Imo	61	13.4
Jigawa	2	0.4
Kaduna	4	0.9
Kogi	2	0.4
Kwara	9	2.0
Niger	3	0.7
Ogun	4	0.9
Ondo	7	1.5
Osun	15	3.3
Oyo	2	0.4
Plateau	11	2.4
Rivers	158	34.8
Other countries -Ghana	2	0.4
Total	454	100.0



Picture 2: map of Nigeria showing the distribution of the state of origin of the study population

Indications for screening for viral Hepatitis B

The indications for screening are shown in table 4. Incidental finding which makes up 64% of the indications include pre-employment screening, pre-marriage screening, screening before blood donation, pre-surgery screening for non-Hepatic related diagnosis and public health awareness campaigns by non-governmental organizations and individuals.51(11.3%) of the study population presented late with advanced Liver disease and 20 (4.4%) were diagnosed from the compulsory antenatal screening done in our institution.

Indication	Frequency (%)
Abdominal pain	58(12.8)
Abdominal swelling	2(0.4)
Antenatal screening	20(4.4)
Febrile illness	18(4.0)
Malaise	2(0.4)
Incidental finding	291(64.0)
Suspected liver disease	51(11.3)
Others	12(2.6)

Table 4: Indications for screening for Hepatitis B

Laboratory (virologic) parameters

HBeAg negative category was predominant compared to HBeAg positive {430(94.7%) vs 24(5.3%)} in our cohort while the HBV DNA (Viral load) ranged from <20 to 170500000iu/ml with a mean value of 4509723.97 ± 26264722.07 and a median value of 1130.50. Undetectable levels of HBV DNA were observed in 8.4% of the study population and lower values of HBV NDA were observed in HBeAg positive individuals than HBeAg negative persons ($\chi 2=6.823$, $p=0.033$). see table 5

Increased AST levels were observed in 256(56.4%) persons while ALT was Increased in 193(42.5%) persons. Comparing the mean of AST to ALT, the mean of the AST levels was notably higher than that of the ALTthough their ranges were comparable. (AST mean 53.905±66.10, range 4.0 to 544.0: ALT mean 42.88±49.57, range 3.0 to 544.0).

Table 5: HBV DNA levels and E antigen comparison

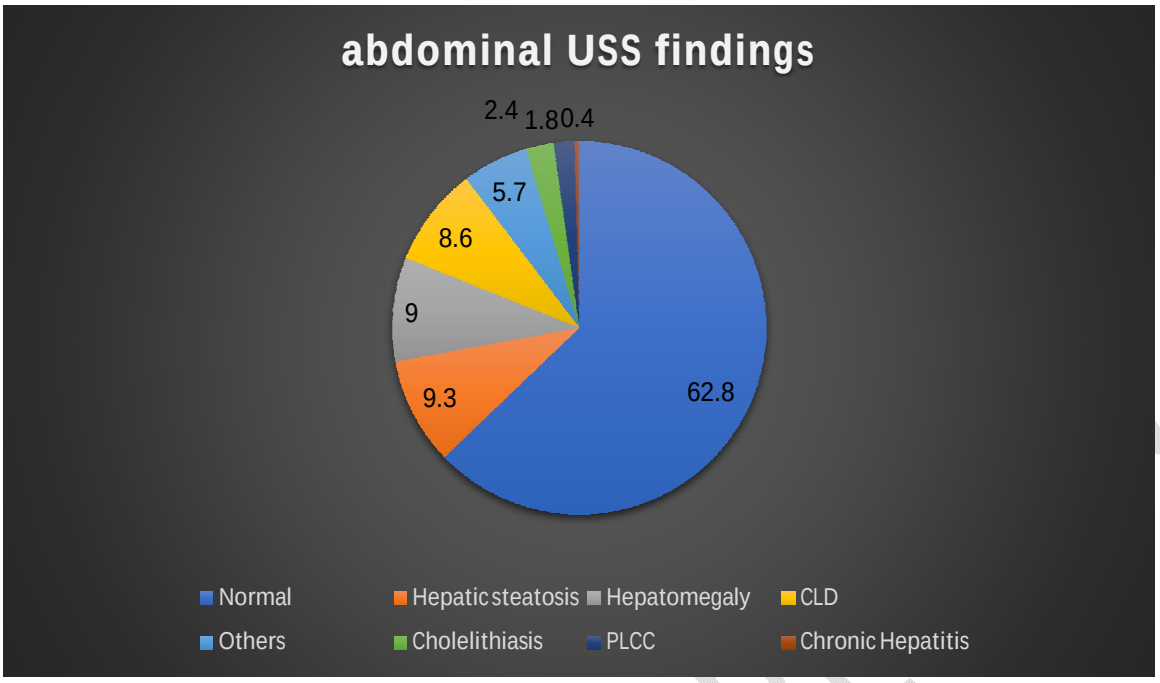
	Undetectable	Low	High
	HBV DNA		
Number	38	224	192
Frequency %	8.4	49.3	42.3
	Eantigen	***comparison***	
E antigen negative	35	207	188
E antigen positive	3	17	4
Total	38	224	192

$\chi 2=6.823$, $p=0.033$

low HBV DNA= <2000iu/ml, high HBV DNA= ≥2000iu/ml, undetectable HBV DNA = < 20iu/ml

Radiological features of the study population

An abdominal ultrasound scan was done routinely at the first visit and the results are shown in picture 2. While more than half of the study population had normal findings, hepatobiliary disorders were discovered in a significant number of the patients ranging from Hepatic steatosis 42(9.3%), Hepatomegaly 41(9.0%), Chronic liver disease39(8.6%), Cholelithiasis 11(2.4%), Chronic hepatitis 2(0.4%) and Primary Liver cell carcinoma in 8 (1.8%). Other reported findings on abdominal USS include bilateral renal parenchymal disease, Hydronephrosis, isolated Splenomegaly and Cystitis and these were described in 2.6% (12) of the study population.



Picture 2: Abdominal ultrasound scan findings. PLCC= Primary Liver cell carcinoma. CLD= Chronic Liver Disease.

Discussions

This studyaimed at an in-depth analysis of the indications for screening, and the sociodemographic, virologic and radiologic characteristics ofthe HBV population.

The study revealed a gender disparity in the prevalence of hepatitis B, with more males being affected than females among adults. This observation aligns with previous studies that have also reported a higher prevalence of hepatitis B among males compared to females. (19,20) Multiple studies have also reported a male predominance in the distribution of hepatitis B infection especially in the adult population. (19–22) A Zambian study reported a male-to-female carrier state of 14.6% to 4.6% for HbsAg and 82.6% of the male population were positive for at least one marker compared to 69.4% of females. (23)The mean age of the study population was 38.33years with >78% being young adults (table 1)similar to figures reported by other African investigators. (24,25)

Several factors could contribute to this gender disparity. One possible explanation is differences in behaviors and risk factors between males and females. For example, males may be more likely to engage in high-risk behaviors such as intravenous drug use or unprotected sex, which can increase the risk of hepatitis B transmission. Additionally, cultural and societal factors may also play a role, influencing healthcare-seeking behaviors and access to screening and vaccination services.

Understanding these gender disparities is crucial for developing targeted prevention and intervention strategies to reduce the burden of hepatitis B, particularly among males who are disproportionately affected. Further research is needed to explore the underlying reasons for this gender disparity and to develop effective public health interventions aimed at reducing the prevalence of hepatitis B among males.

Geopolitically, all six geopolitical zones of the country and >2/3rd of the 36 states of Nigeria are represented in this study demonstrating the metropolitan nature of the study site. The higher representation from the south-south zone can be explained by the high population of Locals as well as persons from nearby states residing in Rivers state. This picture is expectedly in contrast withthe 2021 review and meta-analysis on HBV in Nigeria that recorded the North-West zone as having the highest prevalence of viral Hepatitis B (26) due to multiple factors including low immunization coverage, geographical isolation, and birthing outside healthcare facilities.

The study observed a varied array of reasons for HBV screening ranging from non-health issues which were tagged as incidental indications to hepatic and non-hepatic related diseases. Sixty-four percent (64%) of the study population were diagnosed with viral hepatitis B incidentally while a considerable percentage were diagnosed with HBV during an illness with ≥ 11% exhibiting clinical features of liver disease already. Persons who presented to the clinic for pre-employment medical examination, pre-marriage screening, screening before blood donation, pre-surgery screening for non-Hepatic related diagnosis and public health awareness campaigns by non-governmental organizations, were screened for viral hepatitis B with some turning out positive. This finding underscores the importance of routine screening among this population. This strengthens the need for the prioritization of viral hepatitis B by the government and aid agencies and the need for the development and implementation of an effective public health strategy towards the 2030 WHO elimination goals for viral Hepatitis. (26,27)

Assessment of the characteristics of the Hepatitis B virus in the study population revealed that 94.7% were HBeAg negative compared to HBeAg positive with a few numbers (n=38) of the patients having undetectable HBV DNA. Furthermore, among the 194 patients with high HBV DNA levels, 97.9% (n= 188) were HBeAg negative (p= 0.033). Studies have however shown that HBeAg negative chronic HBV is the most predominant form of the disease worldwide (27,28,29) and HBeAg-negative/anti-HBe-positive chronic hepatitis B (CHB) are more common in Africa due to the molecular characteristics of the prevailing HBV genotype. (7)

Notably, 42.5% of the patients have elevated ALT levels indicating some degree of necroinflammation. ALT could provide a sensitive alternative to liver biopsy in the assessment of hepatic inflammation and a cheaper alternative to HBV DNA is lacking hence determining when to initiate therapy for chronic HBV patients.

Conclusion

This study analyzed the indications for hepatitis B screening and the characteristics of the HBV population, revealing a gender disparity with more males affected than females. The majority of the participants were diagnosed incidentally or during an illness, highlighting the importance of routine screening. Additionally, the study found that the majority of patients had HBeAg-negative chronic HBV, indicating the need for effective public health strategies to address this prevalent form of the disease. Additionally, a significant percentage of patients had elevated ALT levels, suggesting hepatic inflammation, emphasizing the importance of ALT as a marker for HBV-related liver disease.

Overall, these findings emphasize the need for targeted prevention and intervention strategies to reduce the burden of HBV, particularly among males who are disproportionately affected. Further research is needed to explore the underlying reasons for the gender disparity and to develop effective public health interventions aimed at reducing the prevalence of HBV.

Limitations

This study has some limitations. It is a single-centrehospital-based study and thus may not capture the enormity of the burden of chronic hepatitis Bin the general population in Nigeria.

Recommendations

Despite the high prevalence of viral hepatitis B in Nigeria, we are yet to have a comprehensive and effective care package for patients living with viral Hepatitis. Thus, the recommendation to the federal government of Nigeria and other relevant bodies is to make HBV a priority by improving screening and increasing access to care. There is a needfor a global and locally domiciled plan for HBV care including education, population-based surveys as against sporadic hospital/healthcare facility-based reports and unitary, unabridged and full funding for HBV care in Nigeria.

Pre-employment medical examination, pre-marital screening should be made compulsory by law. This will improve the screening yield of viral hepatitis B infection.

The relevant health authorities need to adopt ‘point of care’ (POC) tests for HbsAg and HCV antibodies at the community level as well as POC for cheaper and easy HBV DNA quantification as a means of treatment evaluation.

Other important measures include improving and implementing the test-and-treat strategy for HBV-infected pregnant women, and improving access to birth dose immunoglobulin and neonatal vaccination.

Furthermore, HBV prevention and care should be integrated into all health sectors be it public or private. Bloodfor donation should be screened with the triple panel screening kit rather than the regular RDTs and ELISA tests as these have a low sensitivity and are unable to screen HBV mutant strains.

Competing interest

The authors declare no conflict of interest

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