Scientific African 5 (2019) e00121

Contents lists available at ScienceDirect

Scientific African

journal homepage: www.elsevier.com/locate/sciaf

Markers of hepatitis B virus infection in a subset of young people in central Nigeria

Haruna I. Mohammed [a], Grace R. Pennap [a], Victor B. Oti [a], Moses P. Adoga [a,b,*]

[a] Department of Microbiology, Nasarawa State University, P.M.B. 1022, Keffi, Nigeria
[b] International Centre for Infection and Biomolecular Science (ICIBS), Nasarawa State University, Keffi, Nigeria

ARTICLE INFO

Article history:
Received 3 January 2019
Revised 6 July 2019
Accepted 6 August 2019
Available online xxx

Keywords:
Hepatitis B virus
Hepatitis B core antibody
Hepatitis B e antigen
Hepatitis B surface antibody
Hepatitis B e antibody
Nigeria

ABSTRACT

Hepatitis B virus (HBV) is 50–100 times more infectious than HIV, and hepatitis B is endemic in Nigeria. In this study, we evaluated the serologic markers of HBV infection and associated socio-demographic factors in a subset of young people in Central Nigeria. Blood samples were collected from 350 consenting newly admitted students of the 2016/2017 academic session of Nasarawa State University, and their socio-demographic information obtained using structured questionnaires. The sera were analysed for HBsAg, HBsAb, HBcAb, HBeAg and HBeAb using a 5-panel HBV profiling diagnostic kits (Qingdad High Top Biotech Co. Ltd, Hangzhou, China). Data was analysed using Smith's Statistical Package (version 2.80, California, USA); and test of significance performed at 95% confidence limit with P values ≤ 0.05 considered significant. Of the 350 participants, 157 (44.9%) were male and 193 (55.1%) were female. Overall, 34 (9.7%) had HBsAg, 134 (38.3%) had HBsAb, 98 (28.0%) had HBcAb, 13 (3.7%) had HBeAg and 16 (4.6%) had HBeAb. Gender distribution showed that 20 (12.7%), 78 (49.7%), 59 (37.6%), 9 (5.7%) and 11 (7.0%) of male subjects had HBsAg, HBsAb, HBcAb, HBeAg and HBeAb respectively. Among female subjects, the distribution of HBsAg, HBsAb, HBcAb, HBeAg and HBeAb was 14 (7.3%), 56 (29.0%), 39 (20.2%), 4 (2.1%) and 5 (2.6%), respectively. Being male, unmarried and histories of alcohol consumption, blood transfusion, sharing of sharp objects and multiple sex partners were significant predictors of infection ($p < 0.05$). This study reveals high prevalence of HBV and risk of transmission in the apparently healthy freshmen. Our findings have critical implications for intervention initiatives especially among students and youths.

Introduction

Hepatitis B virus is 50–100 times more infectious than HIV; and it is the aetiologic agent of hepatitis B, an infection that is endemic in Nigeria [1–4]. HBV is a double-stranded DNA virus of a complex structure that causes infection of the liver [5]. The virus belongs to the *Hepadnaviridae* family and is the most common cause of chronic liver disease; hepatocellular carcinoma and necrotizing vasculitis [6]. HBV can cause both acute and chronic infections; and during the acute phase

* Corresponding author at: Department of Microbiology, Nasarawa State University, P.M.B. 1022, Keffi, Nigeria.
E-mail address: adogamoses@yahoo.com (M.P. Adoga).

https://doi.org/10.1016/j.sciaf.2019.e00121

of infection, symptoms are not experienced by most people. Nevertheless, certain individuals develop acute illness with symptoms that last several weeks, including yellowing of the skin and eyes (jaundice), nausea, dark urine, extreme fatigue, abdominal pain and vomiting [7]. Additionally, in individuals with acute hepatitis, a small subset can develop life-threatening acute liver failure whereas in certain individuals, HBV establishes a chronic liver infection that progresses to cirrhosis or cancer of the liver [2,7].

According to the WHO's 2017 global hepatitis report (the latest and first such report by the WHO), 257 million people were living with chronic HBV infection in 2015, with African and Western Pacific regions accounting for the highest burden [8]. In Nigeria, hepatitis B prevalence ranges from 4–32% depending on the subject population [1,2,5,9–11].

Laboratory diagnosis of HBV includes detection of markers such as HBsAg, HBsAb, HBcAb, HBeAg and HBeAb in the serum [12]. Detection of HBsAg in the serum is indicative of HBV infection and this marker is the most frequently used in testing for HBV infection [13]. HBsAg is detected within 10 weeks in the serum following exposure to the virus and its persistent presence for longer than 6 months may depict chronic infection [14]. Additionally, new HBV infection in certain individuals evolves into chronic infection, whereas there's a spontaneous clearance of the virus in others, with the risk of developing chronic infection being highest in children [8]. As such, the focus of prevention of HBV infection is on children below five years of age, and children five years of age who test positive for HBsAg have chronic infection [8].

The presence of antibody to hepatitis B surface antigen (HBsAb), a neutralizing antibody, suggests recovery and protective immunity against the viral infection. It is the only detectable marker in those who respond to hepatitis B vaccine successfully [15]. On the other hand, serum hepatitis B envelope antigen (HBeAg) is associated with active HBV replication and transmission of infection [16].

Moreover, an individual may harbour HBV infection for 30 years or more before the manifestation of clinical symptoms [8]. Remission of disease is associated with sero-conversion from HBeAg to HBeAb and serum disappearance of HBV DNA [17]. Although hepatitis B core antigen (HBcAg) is not found in serum because it is an intracellular antigen, the serum antibody to hepatitis B core antigen (HBcAb) symbolizes an earlier contact with the virus [18,19]. During early HBV infection, the IgM anti-HBc first appears in the serum; and this is usually detected within one month after appearance of HBsAg [20,21]. The presence of IgG anti-HBc, which is not a neutralizing antibody, remains for life in both acute and chronic cases of infection. However, in the absence of circulating HBsAg, the presence of IgG anti-HBc in the serum may suggest an occult HBV infection in persons positive for serum HBV DNA irrespective of other HBV serologic markers [20].

Although HBV infection is endemic in Nigeria, the epidemiology of the virus among young people and student populations is poorly understood across the country in spite of the significance of this in designing effective intervention initiatives. In this study, we therefore, identified the serologic markers of HBV infection and analysed associated socio-demographic factors in a subset of young individuals in Central Nigeria. We found that the prevalence of HBsAg was high and the risk of transmission, denoted by the prevalence of HBeAg, was significant in this population. Our findings will bolster understanding of the epidemiology of the virus especially in Nigeria, with implications for intervention initiatives that include designing effective treatment and prevention policies.

Materials and methods

Study area and population

This study was conducted in Nasarawa State University, Keffi (NSUK), Nasarawa State, Nigeria. NSUK is a higher educational institution with a student population that is well above twenty thousand. The institution offers both undergraduate and postgraduate programmes with a blend of both local and foreign students. Keffi city is approximately 68 km from Abuja, the capital city of Nigeria and 128 km from Lafia, the capital city of Nasarawa State. It is located between Latitude 8°5 N of the equator and Longitude 7°8 E and situated on an altitude of 850 m above sea level [21]. The study recruited 350 newly admitted undergraduate students of the 2016/2017 academic session who gave informed consent for their participation. A representative sample size was determined using the formula propounded by Naing [22]. Socio-demographic information was obtained by administering a structured questionnaire.

Sample collection

Three mls of blood was obtained from each participant by venepuncture and placed in an appropriately labelled plain tube. This was allowed to clot at room temperature and spun for 5 min at 3000 rpm. The resultant sera were harvested into well-labelled cryovials and stored at −20 °C until use.

Laboratory analysis

Detection of HBV serologic markers

To detect HBV serologic markers (HBsAg, HBsAb, HBeAg, HBeAb and HBcAb), a 5-panel HBV test kit (Qingdad High Top Biotech Co. Ltd, Hangzhou, China) was used. Test and result interpretations were carried out according to the manufacturer's instructions.

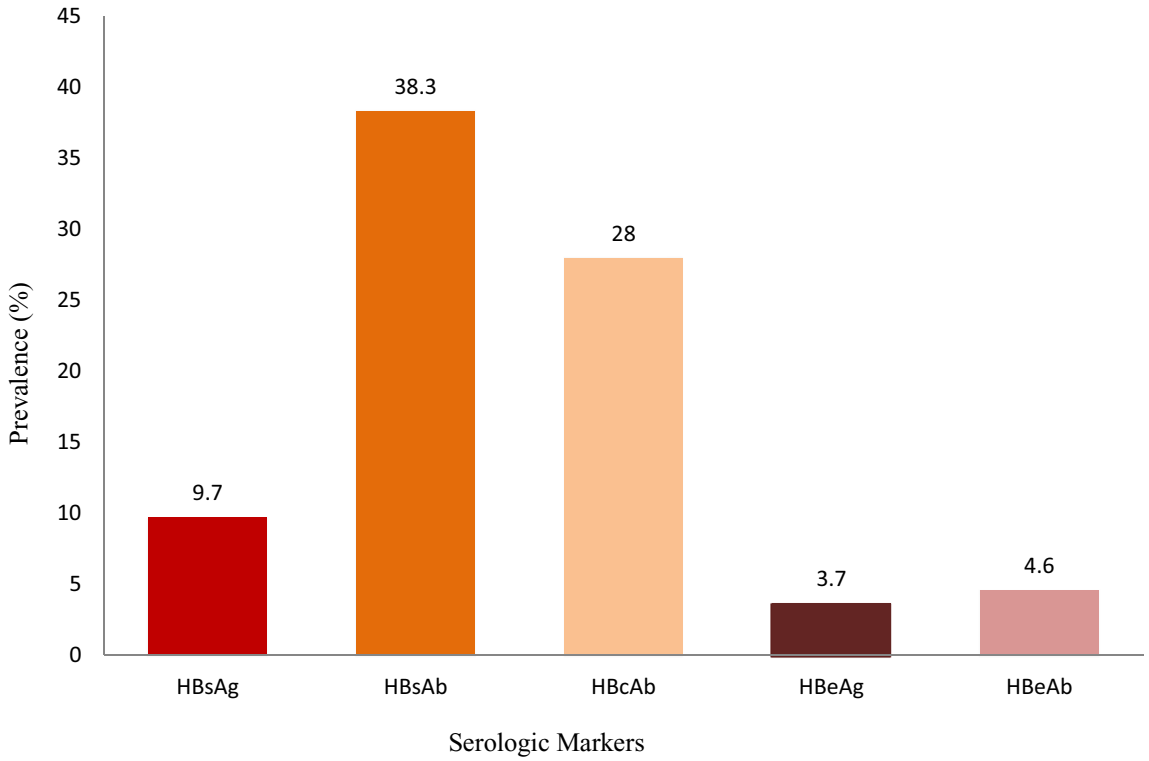

Fig. 1. Distribution of HBV serologic markers among a subset of apparently healthy young people in Central Nigeria.

Table 1
Pattern of serologic markers for HBV infection in a subset of apparently healthy young people in central Nigeria.

Pattern of HBV serologic markers	Interpretation	Prevalence (%)
$HBsAg^+$, $HBsAb^-$, $HBcAb^+$, $HBeAg^+$, $HBeAb^-$	Chronic infection with high viral replication	4 (1.1)
$HBsAg^+$, $HBsAb^-$, $HBcAb^-$, $HBeAg^+$, $HBeAb^-$	Acute infection with high viral replication	9 (2.6)
$HBsAg^+$, $HBsAb^-$, $HBcAb^+$, $HBeAg^-$, $HBeAb^+$	Carrier with low viral replication	16 (4.6)
$HBsAg^+$, $HBsAb^-$, $HBcAb^-$, $HBeAg^-$, $HBeAb^-$	Recently vaccinated	5 (1.4)
$HBsAg^-$, $HBsAb^+$, $HBcAb^-$, $HBeAg^-$, $HBeAb^-$	Immune due to vaccination	56 (16.0)
$HBsAg^-$, $HBsAb^+$, $HBcAb^+$, $HBeAg^-$, $HBeAb^-$	Immune due to previous natural exposure	78 (22.3)
$HBsAg^-$, $HBsAb^-$, $HBcAb^-$, $HBeAg^-$, $HBeAb^-$	Unexposed	182 (52.0)
Total		350

Ethical clearance

Ethical approval for this study (Ref: FMC/KF/HREC/171/17) was obtained from the Health Research Ethics Committee (Reg. No. NHREC/21/12/2012) at the Federal Medical Centre, Keffi, Nasarawa State, Nigeria.

Statistical analysis

Data obtained was subjected to descriptive statistical analysis using the Smith's Statistical Package Version 2.80 (Claremont, California, USA). Chi-squares (χ^2) were calculated and P values obtained at 95% confidence interval; with P values $\leq$0.05 considered statistically significant.

Results and discussion

A total of 350 newly admitted undergraduate students of Nasarawa State University, Keffi, with a mean age of 22.2 years voluntarily participated in this study. Of these, 34 (9.7%) were positive for HBsAg, 134 (38.3%) had HBsAb, 98 (28.0%) showed evidence of HBcAb, 13 (3.7%) were positive for HBeAg and 16 (4.6%) had HBeAb (Fig. 1).

The patterns of infection markers among the participants (Table 1) show that 4 subjects (1.1%) had chronic infection with high viral replication, 9 (2.6%) had acute infection, 16 (4.6%) were carriers with low viral replication, 5 (1.4%) were recently

Table 2
Socio-demographic factors associated with serologic markers for HBV infection in a subset of apparently healthy young people in central Nigeria.

Age (Years)	No. examined	Prevalence (%)				
		HBsAg	HBsAb	HBcAb	HBeAg	HBeAb
15–19	83	9(10.8)	20(24.1)	17(20.5)	2(2.4)	2(2.4)
20–24	186	17(9.1)	59(31.7)	42(22.6)	6(3.2)	8(4.3)
25–29	63	7(11.1)	46(73.0)	29(46.0)	4(6.3)	5(7.9)
≥30	18	1(5.6)	9(50.0)	10(55.6)	1(5.6)	1(5.6)
***P* value**		**0.1239**	**1.0000**	**0.9617**	**0.5509**	**0.2793**
Gender						
Male	157	20(12.7)	78(49.7)	59(37.6)	9(5.7)	11(7.0)
Female	193	14(7.3)	56(29.0)	39(20.2)	4(2.1)	5(2.6)
***P* value**		**0.0044***	**0.9123**	**0.9124**	**0.0594**	**0.0067***
Marital status						
Unmarried	304	30(9.9)	115(37.8)	84(27.6)	12(3.9)	14(4.6)
Married	46	4(8.7)	19(41.3)	14(30.4)	1(2.2)	2(4.4)
***P* value**		**0.0203***	**1.0000**	**0.1972**	**0.0594**	**0.1090**
History of blood transfusion						
Yes	47	5(10.6)	19(40.4)	11(23.4)	1(2.1)	2(4.3)
No	303	29(9.6)	115(37.9)	87(28.7)	12(3.9)	14(4.6)
***P* value**		**0.0052***	**1.0000**	**0.7634**	**0.0594**	**0.0076***
Multiple sex partners						
Yes	15	3(20.0)	2(13.3)	3(20.0)	1(6.7)	1(6.7)
No	335	31(9.3)	132(39.4)	95(28.4)	12(3.6)	15(4.5)
***P* value**		**0.0044***	**0.7806**	**0.9101**	**0.0594**	**0.0071***
Scarification mark						
Yes	126	14(11.1)	53(42.1)	40(31.8)	5(3.9)	6(4.8)
No	224	20(8.9)	81(36.2)	58(25.9)	8(3.6)	10(4.5)
***P* value**		**0.0045***	**0.9724**	**0.9671**	**0.2058**	**0.0067***
Alcohol Consumption						
Yes	81	6(7.4)	32(39.5)	20(24.7)	2(2.5)	1(1.2)
No	269	28(10.4)	102(37.9)	78(29.3)	11(4.1)	15(5.6)
P		**0.0044***	**0.9701**	**0.9724**	**0.0606**	**0.0071***
Sharing of sharp objects						
Yes	39	4(10.3)	15(38.5)	14(35.9)	1(2.6)	1(2.6)
No	311	30(9.7)	119(38.3)	84(27.0)	12(3.9)	15(4.8)
***P* value**		**0.0017***	**0.9735**	**0.9723**	**0.0594**	**0.0071***
Sharing of clothes and bed space						
Yes	8	8(8.9)	28(31.5)	25(28.1)	2(2.3)	0(0.0)
No	261	26(9.9)	106(40.6)	73(27.9)	11(4.2)	16(6.1)
***P* value**		**0.1573**	**0.9748**	**0.9712**	**0.0606**	**–**
History of HBV infection in the family						
Yes	30	4(13.3)	13(43.3)	14(46.7)	2(6.7)	4(13.3)
No	261	25(9.6)	99(37.9)	71(27.2)	9(3.5)	11(4.2)
Unaware	59	5(8.5)	22(37.3)	13(22.0)	2(3.4)	1(1.7)
***P* value**		**0.1861**	**0.9991**	**0.8493**	**0.0694**	

vaccinated, 56 (16.0%) were immune due to vaccination, 78 (22.3%) were immune due to natural exposure to the virus while 182 (52.0%) have never had any exposure to the virus.

Table 2 shows the socio-demographic factors associated with serologic markers for HBV infection among the apparently healthy young participants. Of the 350 participants, 157 (44.9%) were male and 193 (55.1%) were female. Overall, 34 (9.7%) had HBsAg, 134 (38.3%) had HBsAb, 98 (28.0%) had HBcAb, 13 (3.7%) had HBeAg and 16 (4.6%) had HBeAb. Gender distribution showed that 20 (12.7%), 78 (49.7%), 59 (37.6%), 9 (5.7%) and 11 (7.0%) of male subjects had HBsAg, HBsAb, HBcAb, HBeAg and HBeAb respectively. Among female subjects, the distribution of HBsAg, HBsAb, HBcAb, HBeAg and HBeAb was 14 (7.3%), 56 (29.0%), 39 (20.2%), 4 (2.1%) and 5 (2.6%) respectively. Being male, unmarried and histories of alcohol consumption, blood transfusion, sharing of sharp objects and multiple sex partners (Table 2) were significant predictors of infection ($p < 0.05$).

The 9.7% proportion of individuals who had HBsAg as our findings reveal, demonstrates that the prevalence of HBV in the population was high based on the World Health Organization's classification of prevalence into low (<2%), moderate (2–8%) and high (>8%). Previous studies in Nigeria have illustrated similarly high prevalence in student populations. For example, reported prevalence have included 9.2% among students of a tertiary institution in North Western Nigeria; 11.5% among students of Nasarawa State University, Nigeria; 12.0% among asymptomatic students of Ahmadu Bello University, Nigeria; 15.5% among medical students of Usman Danfodio University, Nigeria; and 31.5% among apparently healthy students of a tertiary institution in North Eastern Nigeria [10,23–26]. Obviously, these findings suggest that hepatitis B is endemic in Nigeria. However, it is likely that the reported varying rates from the different studies were impacted by sample size and study population type.

In contrast, some other studies have reported relatively low prevalence of 4.1%, 4.7%, 6.5% and 8.0% in varying populations of adolescents, university students, school children and pregnant women respectively, in certain parts of Nigeria [5,9,27,28]. Sample size, sample population and the varying levels of engagement in risk predisposing practices across populations and communities might account for the variations in findings [23].

Our evaluation further reveals that 134 (38.3%) of the participants had HBsAb (and as a result were HBsAg negative) either due to vaccination or previous natural exposure to the virus (Table 1), with 78 (22.3%) of them belonging to the latter category; indicating that 22.3% of the study subjects had their infections resolved after natural exposure to the virus. These findings are consistent with the 22.7% prevalence of HBsAb reported among healthy individuals in Benue, Nigeria; 22.2% among surgeons in Lagos, Nigeria; and 28% among hospital personnel in Cairo, Egypt [29–31].

The detection of HBcAb in 28.0% of the participants implies earlier exposure to the virus by this proportion of the participants. However, some studies have reported higher prevalence of HBcAb in certain populations [20,29,30,32]. Differences in sample populations between the studies may account for the variation in findings. Additionally, a study reported by Sadoh and colleagues in 2013 found an 11.4% HBcAb prevalence in a population of infants in Benin [33]. It is instructive that the Benin study was among an infant population in contrast to ours that was among a population of teenagers and young adults. Therefore, the comparatively lower prevalence in the Benin study might be attributed to the age differences between the two populations.

We found that 3.7% of the participants had HBeAg. Since this marker is indicative of active replication and transmission, there was a significant risk of transmission in this population with a potential impact on the incidence of the disease and a concomitant challenge to control initiatives. It has been established that HBsAg-positive individuals, who are as well HBeAg positive, have 70–90% chances of transmitting the virus to their contacts in addition to being at high risk of developing persistent liver disease leading to cirrhosis and primary liver cancer if not treated [17,32,34]. Moreover, studies in other populations have found higher HBeAg prevalence of 6.5% and 4.7% among pregnant Nigerian women and a set of individuals who were HBsAg positive [12,32]. However, a lower rate of 2.7% was reported in one study in Benue State, Nigeria [29]. The reason for these differences may not be unrelated to the fact that the studies were conducted in different populations and as such population differences should understandably impact the outcome. As a further support to this explanation, while the study by Odimayo and colleagues included only individuals who were seropositive for HBsAg [12], our study consisted of apparently healthy individuals.

HBeAb is the antibody produced against HBeAg and its presence denotes low infectivity and transmission of the virus or remission of disease [17]. In other words, just like the HBsAb, its presence most likely indicates recovery from HBV infection [19]. We found a prevalence of 4.7% of HBeAb among the participants. This is lower than the 8.0% reported in 2016 by Odimayo and colleagues among HBsAg seropositive individuals, 13.0% by Mbaawuaga and colleagues and 51.6% by Abah and Aminu among a population of pregnant women in Nigeria [12,29,32]. Differences in study populations may account for the observed differences in findings.

HBV serologic markers say a lot about the prognosis of hepatitis B [35]. Overall, 1.1% of the participants had chronic HBV infection with high viral replication, 2.6% had acute infection with high viral replication, 4.6% were carriers with low viral replication, 1.4% were recently vaccinated, 16.0% were immune due to vaccination, 22.3% were immune due to previous natural exposure to the virus and the remaining 52.0% have never had any exposure to the virus (Table 1). In contrast, one study in Benue State, Nigeria, reported higher prevalence of 3.8% and 8.7% for chronic and acute infections respectively [29]. The Benue study recruited pregnant women, who should normally have low immunity, and this might have informed the differences in outcome between the study and ours [36].

There was a significant association between gender and prevalence of HBsAg and HBeAb in this study ($p < 0.05$). Although differences in the prevalence of HBsAb, HBcAb and HBeAg were not statistically significant ($p > 0.05$), the prevalence of HBsAg, HBsAb, HBcAb, HBeAg and HBeAb were higher in participants who were male than female. These findings are supported by reports from Isa and colleagues in North Western Nigeria and Pennap et al. in Keffi, Nigeria; but finds little support from findings by Mustapha and Jibrin among HIV patients in Gombe State, Nigeria [23,24,37]. Since our study participants were freshmen who had just left their various homes, the common culture that ensures young women spend most of their times at home on domestic activities with little chances of exposure to risk factors outside of home, while young men have more freedom of movement and association, might account for the higher prevalence of HBsAg in the male than female participants in our study.

This study recorded significant association between marital status and prevalence of HBsAg among the participants ($p < 0.05$). The prevalence of HBsAg was higher among single participants than their married counterparts. This finding finds support in reports by Ejele and colleagues among HIV positive patients in Niger Delta, Nigeria; and Isa et al. in a tertiary institution in North Western Nigeria; the differences in study populations notwithstanding [23,38].

Moreover, history of blood transfusion was significantly associated with the prevalence of HBsAg and HBeAg ($p < 0.05$). Higher prevalence of HBsAg was observed among those who had received blood transfusion at some point in their lives. Until recently in Nigeria, testing of blood donors for hepatitis B virus infection was not a routine practice in most clinical settings. This finding concurs with a previous finding by Abah and Aminu in Nigeria [32].

The prevalence of HBsAg was significantly higher among participants who had multiple sex partners than those without ($p < 0.05$). This finding is supported by previous findings including reports by Adekunle et al. among blood donors in a tertiary hospital in Nigeria, Pennap et al. among students of a Nigerian tertiary institution and Mboto and Edet among students in University of Uyo, Nigeria [9,24,39]. There was a statistical significant difference between the prevalence of HBsAg and

HBeAb in relation to scarification mark in this study ($p < 0.05$). It was observed that participants with scarification marks were more likely to have HBV infection (HBsAg) than those without. This finding agrees with previous reports [24,28]; and participants in this category were likely from local homes where knowledge of transmission of the virus through the use of sharp unsterilized objects in making body-piercing marks is inadequate or lacking. In addition, alcohol consumption was unexpectedly not significantly associated with infection in this study. This disagrees with previous reports that have designated alcohol consumption as a transmission risk [40,41]. It was possible that the participants in our study were not sincere with their alcohol consumption habits, making our data on this not to be a true reflection of the reality.

Moreover, higher prevalence of HBsAg was recorded among those who shared sharp objects than those who did not. This result is in consonance with other studies done in Nigeria [9,42]; and our findings further confirm that practices such as sharing of sharp unsterilized objects permit transmission of the virus. Additionally, there was no statistical significant association between the prevalence of HBV serologic markers in relation to sharing of clothes and bed spaces among the participants ($p > 0.05$). This finding is supported by reports from Ndako et al. in North Central Nigeria and Isa et al. in North Western Nigeria [23,42]. However, this should not preclude the fact that HBV can be transmitted through those means since the virus can be found in saliva, tears, urine, breast milk and any other body fluid [23].

Although participants who had history of HBV infection in their families had higher prevalence of HBV than those without, this factor was not found to be significantly associated with infection ($p > 0.05$). However, a more robust study design that considers two groups of individuals; one with the history and the other (a control group) without the history will provide a much more reliable result. Generally, our findings and other similar findings [43], raise critical policy questions about intervention programmes that should be designed for students and young people especially in Nigeria and the rest of Africa.

Conclusions

This study reveals high prevalence of HBV and risk of transmission in the apparently healthy freshmen. This is alarming and unacceptable for a disease that has had a vaccine available since 1982. Youth and student populations across the country should be targeted for special, effective intervention initiatives in a comprehensive, holistic intervention programme that includes all populations and individuals of all ages.

Acknowledgement

The study team would like to thank the study participants for their valuable participation. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

[1] M.P. Adoga, E.B. Banwat, J.C. Forbi, L. Nimzing, C.R. Pam, S.D. Gyar, Y.A. Agabi, S.M. Agwale, Human immunonodeficiency virus, hepatitis B virus and hepatitis C virus: sero-prevalence, co-infection and risk factors among prison inmates in Nasarawa state, Nigeria, J. Infect. Dev. Ctries. 3 (7) (2009) 539–547.
[2] M.P. Adoga, S.D. Gyar, S. Pechulano, O.D. Bashayi, S.E. Emiasegen, T. Zungwe, O.H. Iperepolu, C. Agupugo, S.M. Agwale, Hepatitis B virus infections in apparently healthy urban nigerians: data from pre-vaccination tests, J. Infect. Dev. Ctries. 4 (6) (2010) 397–400.
[3] M.P. Adoga, G. Pennap, B.O. Akande, J.P. Mairiga, S. Pechulano, S.M. Agwale, Evaluation of a recombinant DNA hepatitis B vaccine in a vaccinated Nigerian population, J. Infect. Dev. Ctries. 4 (11) (2010) 740–744.
[4] J.C. Forbi, G. Vaughan, M.A. Purdy, D.S. Campo, G.L. Xia, L.M. Ganova-Raeva, S. Ramachandran, H. Thai, Y.E. Khudyakov, Epidemic history and evolutionary dynamics of hepatitis B virus infection in two remote communities in rural Nigeria, PLoS One 5 (7) (2010) e11615, doi:10.1371/journal.pone.0011615.
[5] B.V. Oti, G.R. Pennap, H.R. Ngari, HBsAg and anti-HCV prevalence among pregnant women accessing antenatal care in a tertiary healthcare facility in central nigeria, Hepatol. Pan. Sci. 2 (2018) 110–113.
[6] C.L. Thio, C.A. Hawkins, Hepatitis b virus and hepatitis delta virus, Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases, 8th ed., Elsevier Inc, 2014, pp. 1815–1839. e7, doi:10.1016/B978-1-4557-4801-3.00148-X.
[7] World Health Organization, Hepatitis B, 2018. https://www.who.int/news-room/fact-sheets/detail/hepatitis-b.
[8] World Health Organization, Global Hepatitis Report, World Health Organization, 2017 https://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/.
[9] C.I. Mboto, E.J. Edet, Prevalence and risk factors of hepatitis b virus infection among students in University of Uyo, Int. J. Mod. Biol. Med. 2 (2) (2012) 101–111.
[10] M.Y. Tula, O. Iyoha, A cross-sectional study on the seroprevalence of HBsAg among apparently healthy students of a tertiary institution in north-eastern Nigeria, Int. J. Trop. Dis. Health 7 (3) (2015) 102–108.
[11] G.R. Pennap, B.V. Oti, A.G. Alaribe, S.A. Ajegena, P.R. Galleh, Seroprevalence of hepatitis B and C viruses among HIV infected patients accessing healthcare in federal medical centre, Keffi, Nigeria, J. Adv. Microbiol. 3 (4) (2017) 1–6, doi:10.9734/JAMB/2017/34284.
[12] M.S. Odimayo, S.I. Nwadioha, A.O. Ajayi, Hepatitis B serologic markers among individuals with hepatitis B surface antigen seropositivity in Makurdi, Nigeria, Int. J. Med. Med. Sci. 6 (5) (2016) 340–344.
[13] A.S. Lok, B.J. McMahon, Chronic hepatitis B, practice guidelines committee, American association for the study of liver diseases, Hepatology 34 (2011) 1225–1241.
[14] E.C. Okocha, O.C. Oguejiofor, C.U. Odenigbo, U.C. Okonkwo, Prevalence of hepatitis B surface antigen seropositivity among HIV-infected and non-infected individuals in Nnewi, Nigeria, Niger. Med. J. 53 (4) (2012) 249–253.
[15] Y.S. Chen, X.F. Liang, J.F. Hu, The serum markers of hepatitis B virus (HBV) infection and the natural history of chronic HBV infection, Zhongguo Ji Hua Mian Yi 15 (3) (2009) 279–283.
[16] Centers for Disease Control and Prevention, Hepatitis B, frequently asked questions for health professionals, 2017, https://www.cdc.gov/hepatitis/hbv/hbvfaq.htm#general.
[17] E.E. Mast, C.M. Weinbaum, A.E. Fiore, M.J. Alter, B.P. Bell, L. Finelli, L.E. Rodewald, J.M. Douglas, R.S. Janssen, J.W. Ward, A comprehensive immunization strategy to eliminate transmission of hepatitis b virus infection in the united states: recommendations of the advisory committee on immunization practices (ACIP) part II: immunization of adults, MMWR Recomm. Rep. 55 (RR–16) (2006) 1–33.

[18] F.A. Di Lello, J. Macías, C.C. Cifuentes, J. Vargas, J.C. Palomares, J.A. Pineda, Low prevalence of occult hbv infection among HIV-infected patients in southern Spain, Enferm. Infecc. Microbiol. Clin. 30 (6) (2012) 312–314, doi:10.1016/j.eimc.2011.09.003.
[19] J.H. Kao, Diagnosis of hepatitis B virus infection through serological and virological markers, Expert Rev. Gastroenterol. Hepatol. 2 (4) (2008) 553–562, doi:10.1586/17474124.2.4.553.
[20] J.H. Kao, Role of viral factors in the natural course and therapy of chronic hepatitis B, Hepatol. Int. 1 (4) (2007) 415–430, doi:10.1007/s12072-007-9033-2.
[21] V.L. Akwa, N.L. Binbol, K.L. Samaila, N.D. Marcus, Geographical Perspective of Nasarawa State, Onaive Printing and Publishing Company Ltd, Keffi, 2007, p. 503.
[22] N.N. Naing, Determination of sample size, Malays. J. Med. Sci. 10 (2) (2003) 84–86.
[23] I. Isa, M. Aminu, S.A. Abdullahi, M.A. Sani, M.D. Esona, Seroprevalence of hepatitis B virus in a tertiary institution in north western Nigeria, Afric. J. Microbiol. Res. 9 (3) (2015) 171–179, doi:10.5897/AJMR2014.7068.
[24] G.R. Pennap, O. Nwachukwu, D. Ishaleku, R.J. Ombugadu, Hepatitis B virus carriage among students of a Nigerian tertiary institution. A cohort of eligible blood donors, Res. J. Med. Sci. 5 (2) (2011) 90–93.
[25] M. Aminu, E.E. Okachi, S.M. Abubakar, A. Yahaya, Prevalence of hepatitis B virus surface antigen among healthy asymptomatic students in a Nigerian university, Ann. Afr. Med. 12 (1) (2013) 55–56, doi:10.4103/1596-3519.108257.
[26] M.N. Alo, H.M. Alhassan, A.Y. Saidu, U.I. Ugah, H. Abdulahi, Seroprevalence of hepatitis B surface antigen (HBsAg) among the medical students of usmanu danfodiyo university, Sokoto, Sokoto state, Nigeria, Eur. J. Exp. Biol. 3 (3) (2013) 666–671.
[27] E. Ugwuja, N. Ugwu, Seroprevalence of hepatitis B surface antigen and liver function tests among adolescents in Abakaliki, south eastern Nigeria, Int. J. Trop. Med. 6 (2) (2010) 1–12.
[28] O. Nworie, O.J. Orji, N.N. Ekuma, N.N. Ukpabi, E.N. Onu, Studies on the seroprevalence of HBV among school children in Ohaukwu, Ebonyi state, Nigeria, World Appl. Sci. J. 33 (11) (2015) 1767–1772.
[29] E.M. Mbaawuaga, C.U. Iroegba, A.C. Ike, Hepatitis B virus serological patterns in Benue state, Nigeria, Open J. Med. Microbiol. 4 (2014) 1–10.
[30] A.C. Bello, Prevalence of hepatitis b virus markers in surgeons in Lagos, Nigeria, East Afr. Med. J. 77 (2010) 283–285.
[31] R. Goldsmith, S. Zakaria, M.S. Zakaria, M.A. Mabrouk, A.M. Hanafy, A.H. El-Kaliouby, M. El- Rifae, Occupational exposure to hepatitis B virus in hospital personnel in Cairo, Egypt, Acta Trop. 46 (5–6) (1989) 283–290.
[32] H.O. Abah, M. Aminu, Seroprevalence of hepatitis B virus serological markers among pregnant Nigerian women, Ann. Afr. Med. 15 (1) (2016) 20–27.
[33] A.E. Sadoh, W.E. Sadoh, C.O. Eregie, Serological markers of hepatitis B infection in infants presenting for their first immunization, Niger, J. Paediatr. 40 (2013) 248–253.
[34] D.Z. Egah, E.B. Banwat, E.S. Audu, D. Iya, B.M. Mandong, A.A. Anele, N.E. Gomwalk, Hepatitis Surface Antigen, Hepatitis C and HIV antobodies in low risk blood donor group, Nigeria, East. Mediterr. Health J. 13 (2015) 1–6.
[35] V. Lavanya, T. Viswanathan, S. ArulSheeba, A. Malarvizhi, K. Moorthy, Prevalence of HBV infection among blood donors with antibodies to HBV core antigen, Int. J. Med. Med. Sci. 4 (6) (2012) 128–137.
[36] Z. Williams, Inducing tolerance to pregnancy, N. Engl. J. Med. 367 (2012) 1159–1161.
[37] S.K. Mustapha, Y.B. Jibrin, A.Y. Musa, The prevalence of hepatitis B surface antigenemia in patients with human immunodeficiency virus infection in Gombe, Nigeria, Ann. Afr. Med. 4 (2014) 10–11.
[38] O.A. Ejele, C.A. Nwauche, O. Erhabor, The prevalence of hepatitis B surface antigenaemia in HIV positive patients in the Niger delta, Nigeria, Niger. J. Med. 13 (2) (2004) 175–179.
[39] O. Adekanle, D.A. Ndububa, O.O. Ayodeji, B. Paul-Odo, T.A. Folorunso, Sexual transmission of the hepatitis B virus among blood donors in a tertiary hospital in Nigeria, Singap. Med. J. 51 (12) (2010) 944–947.
[40] I. Mabry-Hernandez, P. Lewis 3rd, Screening for hepatitis B virus infection in nonpregnant adolescents and adults, Am. Fam. Physician 92 (4) (2015) 301–302.
[41] J.S. Esherick, E.D. Slater, J.A. David, Current Practice Guidelines in Primary Care, McGraw-Hill, New York, 2018, p. 230.
[42] J.A. Ndako, O.O. Nwankiti, G.O. Echeonwu, S.A. Junaid, O. Anaele, T.J. Anthony, Studies on prevalence and risk factors for hepatitis *B* surface antigen among secondary school students in north-central Nigeria, S. J. Biomed. Res. 3 (3) (2011) 163–168.
[43] Z.Y. Lado, C.C. Ogbaga, O.F. Nwagbara, Epidemiology of hepatitis B viral infection among students and non-teaching (casual) staff of Nile university of Nigeria: a 2017 study, J. Pub. Health Epidemiol. 10 (3) (2018) 77–86.