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Serological markers of HBV infection: A community-based study of urban dwellers in Southwest Nigeria

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Abstract

Background and Aim: Globally, hepatitis B virus (HBV) infection has been a major public health issue. In sub-Saharan Africa, about 10-20% of the general population are chronic carriers of HBV infection thus, making it a high endemic region. This study was designed to evaluate the pattern of distribution of markers of HBV among asymptomatic subjects in an urban community in southwest Nigeria.

Methodology: The study was carried out among apparently healthy subjects without prior knowledge of their HBV status. A structured questionnaire was used to collect demographic and relevant information while ELISA kits were used to detect HBsAg/Ab, HBeAg/Ab, Total antiHBc and antiHBc IgM using the participants' sera.

Results: The results of 438 subjects comprising, 133 (30.4%) males and 305 (69.6%) females were analysed, age ranged 1.5-70 years (35.7±15.7 years). Overall, 31 (7.1%) of the participants had detectable HBsAg, 2 (6.5%) and 7 (1.6%) subjects had detectable HBeAg and anti-HBc IgM respectively. Anti-HBs was detected in 83(18.9%) subjects, while 39 (8.9%) had anti-HBe. Of the HBsAg positive participants, 1 (3.2%) of them was also positive for both anti-HBc IgM and HBeAg, 25 (80.6%) had antiHBe while 3 (9.7%) had only anti-HBc IgM. None of them had antiHBs. Among those who were HBsAg negative, 83 (20.4%) had anti-HBs as the only serological marker, while 313 (76.9%) had no serological markers of HBV infection. Only 145 of the total population were tested for anti-HBc Total, of whom 65(44.8%) were positive.

Conclusion: This study has highlighted the burden of HBV infection in the population studied. There is therefore, the need for more awareness through information programmes to the public and for preventive measures through vaccination programmes.

Keywords: *HBV infection, Serological markers, Urban, Southwest Nigeria*

Résumé

Contexte et objectif : À l'échelle mondiale, l'infection par le virus de l'hépatite B (VHB) a été un problème majeur de santé publique. En Afrique subsaharienne, environ 10 à 20% de la population générale sont donc porteurs chroniques de l'infection par le VHB, ce qui en fait une région fortement endémique. Cette étude a été conçue pour évaluer le modèle de distribution des marqueurs du VHB chez les sujets asymptomatiques dans une communauté urbaine du sud-ouest du Nigéria.

Méthodologie : L'étude a été menée auprès de sujets apparemment sains sans connaissance préalable de leur statut VHB. Un questionnaire structuré a été utilisé pour collecter des informations démographiques et pertinentes tandis que des kits ELISA ont été utilisés pour détecter HBsAg / Ab, HBeAg / Ab, Total antiHBc et antiHBc IgM en utilisant le sérum des participants.

Résultats : Les résultats de 438 sujets comprenant 133 (30,4%) sujets masculins et 305 (69,6%) sujets féminins ont été analysés, l'âge variait de 1,5 à 70 ans (35,7 ± 15,7 ans). Dans l'ensemble, 31 (7,1%) des participants avaient un HBsAg détectable, 2 (6,5%) et 7 (1,6%) sujets avaient respectivement un HBeAg détectable et un IgM anti- HBc. Anti-HBs a été détecté chez 83 (18,9%) sujets, tandis que 39 (8,9%) avaient anti- HBe. Parmi les participants positifs pour HBsAg, 1 (3,2%) d'entre eux était également positif pour IgM anti- HBc et HBeAg, 25

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(80,6%) avaient antiHBe tandis que 3 (9,7%) n'avaient que IgM anti- HBc. Aucun d'eux n'avait d'antiHB. Parmi ceux qui étaient négatifs pour AgHBs, 83 (20,4%) avaient des anti-HBs comme seul marqueur sérologique, tandis que 313 (76,9%) n'avaient aucun marqueur sérologique d'infection par le VHB. Seulement 145 de la population totale ont été testés pour le total anti-HBc, dont 65 (44,8%) étaient positifs.

Conclusion : Cette étude a mis en évidence la charge de l'infection par le VHB dans la population étudiée. Il est donc nécessaire de sensibiliser davantage le public par des programmes d'information et de prendre des mesures préventives par le biais de programmes de vaccination.

Mots-clés : *infection par le VHB, marqueurs sérologiques, urbain, sud-ouest du Nigéria*

Introduction

Globally, Hepatitis B Virus (HBV) infection has been a major public health concern. Over 2 billion of the world's population are infected, among whom, about 257 million are chronic carriers of the virus [1,2]. Majority of these carriers are resident in sub-Saharan Africa and South East Asia [3]. About 25% of chronic carriers of the infection die from its sequelae such as liver cirrhosis, liver failure and hepatocellular carcinoma [4].

Infection at a very young age is more likely to progress to chronicity. Specifically, it has been observed that, about 90% of infected newborns eventually turn out to be chronic carriers [5]. On the other hand, 90-95% of infected adults get rid of the virus with no sequelae, while 5-10% become chronic carriers [6]. However, there are many HBV infected individuals who are asymptomatic carriers living within and cohabiting with other members of the same community especially in endemic areas [2].

In sub-Saharan Africa, about 10-20% of the general population are chronic carriers of HBV infection, thus, making it a high endemic region [1]. It has been observed that at least one marker of HBV infection is found in about 70-95% of adults in this region [7]. HBV has markers of infection found in the blood at different stages which include, hepatitis B surface antigen (HBsAg); antibody to HBsAg (anti-HBs); hepatitis B 'e' antigen (HBeAg); antibody to HBeAg (anti-HBe) and antibody to hepatitis B core antigen (anti-HBc). The presence of any of the markers of infection may signify either infectivity or immune status of such individual [8].

In Nigeria, the prevalence of HBV infection ranges between 9-39% [9-13]. In most studies, HBsAg is the only serological marker used to assess infection, prevalence and endemicity of HBV infection [8,14]. However, the natural history and serology of HBV are complex with multiple laboratory markers. In view of this, this study was designed to evaluate the pattern of distribution of HBV markers of infection among asymptomatic subjects in an urban community in Ibadan, southwestern Nigeria.

Methodology

Study Area: The study was carried out in Ibadan, an urban city in southwest Nigeria. According to the National Population Commission Census of 2006, Ibadan has a population of over 2.5 million people. Majority of the inhabitants of the city are low income earners.

Study Population: The study was carried out among consenting apparently healthy subjects who did not have prior knowledge of their HBV status. Parental accents were sought and obtained for the under aged participants before their enrolment into the study. Participants were educated on HBV infection, risk factors for its transmission, early symptoms of diseases that can result from the infection, as well as ways of preventing the infection.

Data Collection:
A structured questionnaire was used to collect demographic and other relevant information from the participants.

Sample collection and analysis
About 5mLs of venous blood was collected from each participant under aseptic condition. Serum was recovered from each blood specimen by centrifugation for 15 minutes at 1,500 rpm. Recovered sera were transferred into appropriately labelled tubes and then stored at -20°C until analyzed. All samples were tested for HBV markers including HBsAg, antiHBs, HBeAg, anti-HBe, and anti-HBc IgM, using Enzyme Linked Immunosorbent Assay (ELISA) test kits (Diagnostic Automation/Cortez Diagnostic, California, USA). Only 145 samples were screened for anti-HBc-Total using similar kit. Assays were performed in accordance with the manufacturer's instructions. Optical density (OD) was read using the Emax endpoint ELISA microplate reader (Molecular Devices, California, USA) and

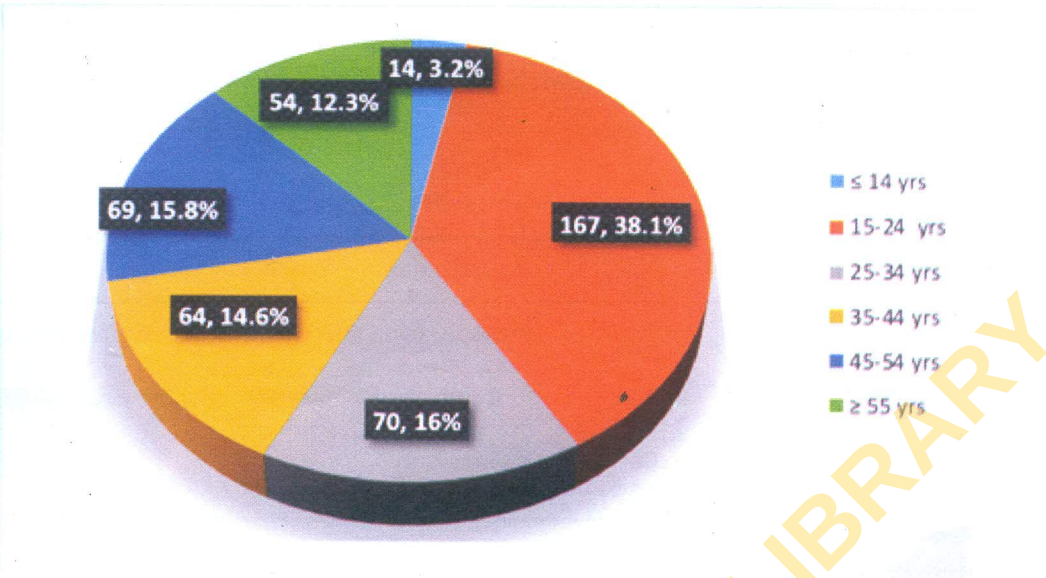

Fig. 1: Frequency and age category of the study participants

subsequently interpreted in line with the manufacturer's instructions.

Data analysis

Data were analyzed using SPSS version 21. Means, charts and tables were used to describe the results with $p<0.05$ considered statistically significant.

Ethical approval

Ethical approvals for the study were granted by the UI/UCH Institutional Review Board (UI/EC/11/0058) and Ministry of Health (AD3/479/349).

mean of 35.7±15.7 years. The analysis showed that, 167 (38.1%) of the subjects were in the age category of 15-24 years, 70 (16%) were in 25-34 age bracket, while 14 (3.2%) were ≤ 14 years (Figure 1).

The frequency of the serological markers of HBV infection is as follows; HBsAg was detected in 31 (7.1%), 19 (61.3%) of whom were in the age range 15-34 years (Table 1). Analysis by gender of those positive for HBsAg showed that 17 (54.8%) were males, while 14 (45.2%) were females and there was significant difference (p= 0.035) between the two

Table 1: Overall age distribution of HBV Markers in the subjects

Age Range (yrs)	No Tested n (%)	HBsAg	HBeAg n (%)	AntiHBe n (%)	AntiHBcIg n(%)	Anti-HBs M n(%)
≤14	14	0(0.0)	0(0.0)	0(0.0)	0(0.0)	5(35.7)
15-24	167	10(6.0)	1(10.0)	12(7.2)	2(1.2)	27(16.2)
25-34	70	9(12.9)	1(11.1)	11(15.7)	2(2.9)	9(12.9)
35-44	64	4(6.3)	0(0.0)	7(10.9)	2(3.1)	11(17.2)
45-54	69	6(8.7)	0(0.0)	6(8.7)	1(1.4)	15(21.7)
≥ 55	54	2(3.7)	0(0.0)	3(5.6)	0(0.0)	16(29.6)
Total	438	31(7.1)	2(6.5)	39(8.9)	7(1.6)	83(18.9)

Results

The results of 438 subjects comprising, 133 (30.4%) males and 305 (69.6%) females were analyzed. Respondents' ages ranged from 1.5–70 years with a

groups. Anti-HBs was found in 83 (18.9%) subjects. Two (6.5%) subjects were HBeAg positive, while anti-HBe was detected in 39 (8.9%) subjects. HBV DNA was detected in 27 (6.2%) subjects, among whom 3

(11.1%) were HBsAg negative. Of the HBsAg positive participants, 1 (3.2%) of them was also positive for both anti-HBc IgM and HBeAg, 25(80.6%) had antiHBe while 3 (9.7%) had only anti-HBc IgM. None of them had anti-HBs (Table 2).

Table 2: Serological profile of HBsAg positive subjects (n=31)

Profile	Additional Marker	n (%)	Interpretation
A1	Anti-HBcIgM, HBeAg	1 (3.2)	Probably acute infection with active viral replication
A2	AntiHBe	25 (80.6)	Probably chronic infection with low viral replication
A3	AntiHBcIgM	3 (9.7)	Probably recent infection
A4	AntiHBs (negative)	0 (0)	No immunity
A5	No other markers	4 (12.9)	Early infection/post vaccination

Among those who were HBsAg negative, 83 (20.4%) had anti-HBs as the only serological marker, anti-HBc IgM and anti-HBe were present in 4 (1.0%) and 14 (3.4%) subjects respectively, while 313 (76.9%) of them had none of the serological markers of HBV infection (Table 3)

Table 3: Serological profiles of HBsAg-negative subjects (n=407)

Profile	Marker	n(%)	Interpretation
B1	HBeAg negative	407(100)	Low replication
B2	AntiHBe	14 (3.4)	Resolved/Low replication
B3	AntiHBcIgM	4 (1.0)	Recent infection
B4	AntiHBs only	83 (20.4)	Post vaccination immunity
B5	No marker	313 (76.9)	Susceptible to infection

Only 145 of the total population sampled were tested for anti-HBc Total. Sixty-five (44.8%) of them were positive. They included 17(11.7%) male and 48(33.1%) female participants in age brackets 20-65 and 18-70 years respectively. Of this subgroup, 15 (10.3%) had HBsAg while twelve (80.0%) out of this number had both anti-HBc and anti-HBe.

Discussion

In this study, an overall prevalence of 7.1% detected for HBV infection is higher than the 4.1-7.0% range reported by Omeje *et al* [15], in Abakaliki in the southeast, Adoga *et al.*[16] in a study among urban dwellers in the North Central and Okonko *et al* 17], among attendees of an STI clinic in Ibadan southwest of Nigeria. This rate is however much lower than 12.6% and 21.3% respectively reported by Jumbo *et al.* [18] in a rural setting and Otegbayo *et al* 19] among blood donors in the same southwest region of the country. The difference in the prevalence rates might be due to the differences in the sample sizes, ethnicity as well as the composition of the study population [15-19]. The rural setting of their study might explain the higher prevalence observed. It is believed that poor awareness and harmful socio-cultural practices in the rural areas might encourage transmission of HBV infection [16]. This was also the observation of Bwogi *et al* [20] in Uganda, in which significantly higher prevalence of HBV infection was found in rural areas. This study also showed a significantly higher prevalence of HBV infection among males compared to females ($p<0.0035$}. This is consistent with the findings of similar studies conducted in Nigeria [21-23], as well as other parts of the world [24].

In this study we found a rate of 6.5% (2/31) for HBeAg (Table 1) and this falls within the range of 6.4- 8.9% reported among blood donors in Nigeria [25-28]. This rate is however lower than the reported 48.4% and 19% HBeAg sero-positivity found among HBsAg-positive patients by Ojo *et al [*29] in Ile-Ife and Ola *et al [*30], in Ibadan respectively in southwest Nigeria and 19.2% HBeAg prevalence found among HBsAg-positive individuals in north-central Nigeria [31]. The lower rate for HBeAg found in this study when

compared with previous findings in southern and Northern regions of Nigeria could be due to the asymptomatic population sampled in our study. It has been documented that active viral replication in liver cells is an indication of the presence of HBeAg found in the serum of individuals infected with HBV which also reflects the presence of HBV DNA as a surrogate marker.[32] Furthermore, studies have also demonstrated that the detection of HBeAg in the serum can serve as a high risk indicator for development of hepatocellular carcinoma [33].

Furthermore, HBeAg virus has been reportedly found in circulation among the general population which serves as a prelude to the endemicity of HBV in Nigeria, and an indicator of active viral replication irrespective of clinical presentation [31]. It also indicates that high infectivity of the virus is widespread among Nigerians with HBV infection [30]. It is therefore advisable to implement routine HBeAg testing for HBV positive patients to ascertain their status of infection for adequate management. In addition, our study detected anti-HBe rate of 8.9% among the study participants. Although this rate may be low, it is however an indication of immune response against the infection and to control its spread. According to earlier report, the presence of anti-HBe may indicate good prognosis and could be suggestive of controlled viral replication in these individuals, since persons with anti-HBe tend to have lower viraemia [34].

In this study, 65(48.8%) of those tested for anti-HBcTotal were positive and by extrapolation, it can be inferred that about half of the study population may have been previously exposed or infected with HBV at one time in their life time. This rate is lower than the 54% reported by Oyero and Omoruyi [35] in a similar study conducted in two urban cities, which also included Ibadan. A rate of 1.6% for anti-HBc IgM found in this study is much lower than 18.4% reported by Jeremiah *et al* [36] among blood donors. The difference in the study population could have explained the difference in the prevalence observed.

Presence of antiHBc in the absence of HBsAg is of great importance in the setting of blood transfusion and organ transplantation because, screening for HBV infection is done mainly with HBsAg, and absence of this does not totally preclude transmission of the infection through blood transfusion or organ transplantation [37]. The same is true for subjects who have HBV DNA but negative for HBsAg. The detection of HBV DNA in serum as the only serological marker suggests occult HBV infection, because individuals with such status are believed to have high viral replication and are highly infectious [26]. Taking cognizance of this scenario will be vital for blood transfusion safety in Nigeria to prevent transmissible blood borne diseases such as HBV.

It was observed that 20.4% of the HBsAg negative subjects had antiHBs as the only serological marker and this could have come from vaccination against HBV infection. This figure is higher than the 6.7% reported by Oyero and Omoruyi [35] in a similar study. It however, showed that vaccine uptake is still very low in our environment and there is need for more awareness. Also observed is that, 76.9% of the subjects had no markers of HBV infection or immunization. This group of subjects is at risk of contracting the infection considering the high prevalence of the infection in the study population. This signifies presence of large number of susceptible members of the study population who are at risk of HBV infection with attendant public health implication. It is therefore pertinent to identify such individuals and vaccinate them so as to control the spread of HBV in the study community [38].

Conclusion

This study has highlighted the pattern of serological markers of HBV infection, as well as the burden of the infection in the study population. It showed that a large number of susceptible individuals of the study population before our intervention were at risk of HBV infection with attendant public health implication. Therefore, there is the need for more awareness to the public about the mode of transmission of HBV and how it can be prevented.

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