AFRICAN JOURNAL OF MEDICINE and medical sciences

VOLUME 41 Second Biomedical Conference Supplement DECEMBER 2012

ISSN 1116-4077

Afr. J. Med. med. Sci. (2012) 41, *Suppl.* 133-137

HBV infectivity among Nigerians

SO Ola[1], JA Otegbayo[1], GN Odaibo[2] and DO Olaleye[2]
Departments of Medicine[1] and Virology[2], College of Medicine, University of Ibadan, University College Hospital, Ibadan, Nigeria.

Abstracts
The study involved 60 (non-immunized), 14 (immunized against HBV), healthy Nigerian adults and 28 Nigerian patients with hepatitis. Their sera were tested for HBsAg, HBeAg, anti-HBe, anti-HBc, anti-HBs and anti-HCV while only 15 subjects with chronic hepatitis had HBV DNA assay by PCR. The subjects aged 21 to 72 years and comprised 75 male and 27 female adults. The prevalence of HBV infection by HBsAg and / or anti-HBc sero-positivity was 55.9%. Only HBsAg and anti-HBs were detectable in 21% each among immunized while HBsAg, HBeAg, anti-HBe, anti-HBc, anti-HBs were present in 58%, 20%, 6%, 32%, and 42% respectively in the non-immunized subjects. HBV DNA was positive in 86.7% of the 15 subjects. About fifty five percent of all subjects were infectious of HBV with 13.7%, 3.9%. 32.3% and 4.9% accounting for high, medium, low and very low infectivity respectively while 44.1% and 1%of the subjects were susceptible and naturally immuned to HBV respectively. Coinfection with HCV tends to favour HBV infectivity. In conclusion, the infectivity of HBV among Nigeria is varied but high and a great proportion of the population is susceptible.

Keywords: *Infectivity, HBV, HCV, Nigerians.*

Résumés
L'étude porte sur 60 nigérians adultes bien portant (non vaccinés), 14 (vaccinés contre le VHB), 28 patients atteints d'hépatite. Leurs sérums ont été testés pour HBsAg, HBeAg, anti-HBe, anti-HBc, anti-HBs et anti-VHC tandis que seulement 15 sujets atteints d'hépatite chronique ont subi le test ADN VHB par PCR. Les sujets âgés de 21 à 72 ans comprenaient 75 hommes et 27 femmes adultes. La prévalence de l'infection par le VHB à partir de la séropositivité au HBsAg et / ou à l'anti-HBc était de 55.9%. Seule l'AgHBs et l'anti-HBs étaient détectables chez 21% des vaccinés alors que chaque HBsAg, HBeAg, anti-HBe, anti-HBc, anti-HBs étaient présents chez 58%, 20%, 6%, 32% et 42% respectivement des sujets non vaccinés. L'ADN du VHB était positif chez 86.7% des 15 sujets. Environ 55 pour cent de tous les sujets étaient infectieux de l'hépatite B à 13.7%, 3.9%. 32.3% et 4.9% ce qui représente la haute, moyenne, faible et très faible infectivité respectivement, tandis que 44.1% et 1% des sujets étaient sensibles et naturellement immunisés contre le VHB, respectivement. La co-infection par le VHC a tendance à favoriser l'infectiosité du VHB.
En conclusion, l'infectiosité du VHB chez les nigérians est variée, mais une forte et une grande proportion de la population y est prédisposée

Correspondence: Dr. S.O. Ola, Department of Medicine, College of Medicine, Universityof Ibadan, University College Hospital, Ibadan, Nigeria. soola@comui.edu.ng., soola2001@yahoo.com

Introduction

Of all the hepatotrophic viruses, hepatic B virus (HBV) is unique in being the only DNA virus and more importantly, it has a peculiar course of infection [1]. The course of the infection depends on age of acquisition of the infection. In addition, it is highly infectious, about 100 times as the human immunodeficiency virus [2]. Nigeria like all other African countries is a hyper endemic nation for the infection; hence its citizens are likely to be exposed to the virus early in life [3]. It is spread by contact as well as by parenteral and sexual routes. These modes of transmission are prevalent among Nigerians [4, 5]. The infection may be asymptomatic or clinical when it could be of anicteric or icteric form. Either type could be acute or chronic during which the infection could also coexist with both the hepatotrophic and the non-hepatotrophic viruses. In view of the varied clinical course of the infection, assay of the serological markers of the virus have varied expressions and patterns [3].

Although, hepatitis B surface antigen (HBsAg) has mostly been determined to reveal the presence of the infection [4-8] but not its infectivity while markers such as hepatitis Be antigen (HBeAg), antibody to HBeAg (anti-HBe) and HBV DNA are indicative of the degree of the contagiousness of the infection. Similarly, antibodies hepatitis B core antigen (anti-HBc) and HBsAg (anti-HBs) are both indicative of previous infection and protection from the infection respectively [9]. Previous reports show assay of HBeAg, antibody to HBeAg (anti-HBe) and HBV DNA has been useful in determining the infectivity of HBV in different populations [9-11].

Despite the hyperendemicity of the infection in Nigeria, its pattern of infectivity is hither to yet undetermined hence the report of our present study of the infectivity of HBV among Nigerians.

Methods

The study involved one hundred and two Nigerians adults consisting of 74 healthy subjects (group 1 with 60 non-immunized – NIM and 14 immuned – IM against HBV) and 28 patients (group 2) with hepatitis. Subjects in groups 1 and 2 were age and sex matched.

The sera of their blood specimens were assayed for hepatitis B surface antigen (HBsAg), hepatitis Be antigen (HBeAg), anti-bodies to HBeAg (anti-HBe), hepatitis B core antigen (anti-HBc), HBsAg (anti-HBs) and hepatitis C virus (anti-HCV) using 3rd generation ELISA Kits at the Department of Virology, University College Hospital, Ibadan. In addition, detection of HBV DNA was also carried out by polymerase chain reaction in only 15 patients with chronic hepatitis using in-house method of a commercial laboratory - Medica (Medizinische Laboratorien Dr F Kaeppeli), Zurich Switzerland.

The study was conducted after ethical clearance was obtained from the UI-UCH Ethical Review Board. The data were analysed statistically with investigation of the significance of any hypothesis by using appropriate statistical test at 5% probability level.

Results

The healthy subjects aged 21-70 years while the patients were 20 -72 years old with male: female ratio of 26:11 and 23:5 respectively, Table1. The detection rates of HBsAg, HBeAg, anti-HBe, anti-HBc, anti-HBs and anti-HCV were 89%, 29%, 48%, 82%, 50% and 21% respectively. The detection rates of only those of HBsAg, anti-HBe, and anti-HBc were significantly higher among the patients than the healthy subjects.Infection with HBV was commoner among all the age groups compared to that of HCV though both infections were preponderant among 21-30 years, Table 2.

Table 1: Age and sex distribution of healthy Nigerian adults and patients with hepatitis.

Group	Male/ Female	Age Range (Mean±SD) years
Healthy Adults (74)	52/22	21-72(34.7±5)
Immunized Adults(14)	10/4	28-61(41.6±7)
Non immunized Adults (60)	42/18	21-72(33.1±4)
Hepatitis (28)	23/5	20 -72(34.2±16)
Total	75/27	20 -72(34.7±8)

Table 3 shows the expression of different patterns of serology markers of HBV among the subjects. The infectivity statuses were high (HBeAg positive), medium (both HBeAg and anti-HBe positive), low (anti-HBe positive), very low (HBsAg and anti-HBc positive), non infectious (anti-HBc and anti-HBs positive) and susceptible (negative for all markers); and they were all present in different proportions of the patients with the exception of the susceptibility status. Of the 15 patients with chronic B who had HBV DNA assay by PCR, HBV DNA was detected among 13 patients who had high (2), medium (2), and low (9) statuses of HBV infectivity while the two patients who were naturally immuned (noninfectious) and HBsAg carrier (very infectivity) were HBV DNA negative.

Although, the immunized and the non immunized subjects against HBV had preponderances of susceptible status in 76.6% and 56.7% respectively, only those with low infectivity status was found the former while the latter had subjects in the different infectivity statuses except the non infectious.

The infectivity rates were 96.4%, 43.3% and 21.4% among the patients, NIM and IM respectively. The very low and non infectious statuses were not found among the female subjects otherwise low

Table 2: Age and gender distribution of HBV and HCV infections among adult Nigerians

Age group	HBV	HCV	HBV + HCV	TOTAL	Types of HBV infectivity					
					H	M	L	VL	N I	S
21-30	25(5)	8(3)	5(2)	36(11)	6(1)	2	14(4)	2	0	12(6)
31-40	22(3)	4(1)	1	47(12)	7(1)	2(1)	11(1)	2	1	24(9)
41-50	2(2)	0	0	9(2)	0	0	4(2)	0	0	5
51-60	6(2)	1	1	6(2)	1(1)	0	3(1)	0	0	2
61-70	1	1	0	3	0	0	0	1	0	2
71-80	1	0	0	1	0	0	1	0	0	0
Total	57(12)	14(4)	7(2)	102(27)	14(3)	4(1)	33(8)	5	1	45(15)

H- High. M – Medium. L – Low. VL – Very Low NI – Noninfectious. S – Susceptible. Parenthesis – females

infectivity status was the commonest irrespective of the groups or gender. In addition, there was no difference in the detection rates of anti-HCV among the healthy (21.4%) and the patients (10.8%). Similarly, HCV infection was present among the different infectivity statuses with the exception of the noninfectious.

Co-infection of HBV and HCV were found only among subjects with high, medium and low infectivity statuses of HBV.

infectivity. Furthermore, presence of both HBeAg and anti-HBe suggests medium infectivity (sero – converting HBsAg to anti-HBe) while anti-HBe suggests previous or recent exposure to HBV infection. The detection of anti-HBe, anti-HBe and HBsAg without HBeAg suggest HBeAg negative HBV (mutant) infection while a subject having anti-HBe, anti-HBe without HBeAg and HBsAg but positive HBV DNA has occult HBV infection [12]. Presence of HBsAg, anti-HBe with or without anti-

Table 3: Serological patterns and infectivity of HBV among Nigeria adults.

Clinical Group (Infectivity Status)	HBs Ag	HBe Ag	Anti-HBe	Anti-HBc	Anti-HBs	HBV DNA* (%)	Number Anti-HCV	Hep	IM	NIM	Male	Female	Percentage Total
Early phase of	+	-	-	-	-		-	1	-	2	2	1	2.9
Infection (Low)	+	-	-	-	+		+2	4	3	12	12	7	18.6
Late Incubation	+	+	-	-	+		-	-	-	2	1	1	2
period (High)	+	+	-	-	-		-	-	-	1	1	-	1
Acute/Chronic HBV	+	+	-	+	-	+(13.2)	-	2	-	-	1	1	2
Infection (High)	+	+	-	+	+		+2	4	-	5	8	1	8.8
Convalescent HBV	+	+	+	+	+		+1	2	-	2	3	1	3.9
infection (Medium)													
HBeAg negative HBV	+	-	+	+	-	+(60)	+1	9	-	-	8	1	8.8
infection (Low)													
Convalescent HBV	-	-	+	+	+	+(6.70	-	1	-	-	1	-	1
infection or HBsAg &													
HBeAg negative HBV													
infection (Low)													
HBsAg & HBeAg	-	-	+	+	-	+(6.7)	-	1	-	-	1	-	1
negative HBV													
infection (Low)													
HBV carrier state (Very Low)	+	-	-	+	+		+1	2	-	2	4	-	3.9
" " " "	+	-	-	+	-	-(6.7μ)	-	1	-	-	1	-	1
Natural immunity to HBV	-	-	-	+	+	-(6.7μ)	-	1	-	-	1	-	1
(Non Infectious)													
Unexposed to HBV	-	-	-	-	-		+7	-	11	34	31	14	44.1
(Suspectible)													
Total Number	54	18	15	32	40	15	102	28	14	60	75	27	102

IM - Healthy adults immunized against HBV NIM – Non-immunized healthy adults
** - HBV DNA assayed in 15 patients with chronic hepatitis μ - HBV DNA negative only*
Hep - Patients with hepatitis

Discussion

Assay of HBsAg has mostly been utilized in the detection of the presence of HBV infection. However, presence of HBsAg does not indicate infectivity hence determination of the contagiousness of subjects with HBV infection needs detection of its markers indicating viral replication such as HBeAg and anti-HBe as well as the isolation of HBV DNA [9]. Presence of HBeAg in a subject is indicative of high infectivity while development of anti-HBe shows low HBs in a subject (HBsAg carrier) and detection of HBV DNA suggests seroconversion making the subject infectious, hence a HBsAg carrier is potentially infectious (very low infectivity) [3, 9, 13].

Our study shows that the assay of only HBsAg does not identify all subjects having HBV infection especially those with occult HBV infection, and natural immunity while assay of both HBsAg and anti-HBc were able to detect all subjects exposed to HBV.

Furthermore, assay of HBeAg and anti-HBe as well as HBV DNA in those sero-positives for HBsAg and or anti-HBc was able to detect the different infectivity statuses [10, 13, 14]. Although about 55% of the entire subjects were infectious, the pattern of distribution was similar among the patients and the non-immunized subjects with descending order of prevalence of low, high, very low and medium infectivities but only those having low infectivity were found among the immunized subjects. This supports the protective effect of vaccination against HBV and shows that HBV is majorly a silent infection among Nigerians with clinical manifestation of sequalae of the infection later in life. Furthermore, the presence of high infectivity among our patients as well as asymptomatic subjects portends a dangerous scenario if immunization is not vigorously pursued, hence the high mortality from preventable hepatocellular cancer among Nigerians [15]. The detection of HBV DNA among our HBV carriers confirms that only some of such subjects are potentially infectious [3, 9, 13] while others are without seroconvertion to HBV replication. In addition, it unveils that a subject symptomatic of hepatitis could be HBsAg sero-negative but anti-HBc positive and still be infectious of HBV especially when HBV DNA positive (occult HBV infection) [16]. This shows some Nigerian patients must have hither to be misdiagnosed as not having HBV infection with the assay of only HBsAg as the surrogate marker for HBV infection [5].

The assay of anti-HBs among our subjects helps to identify a subject who has developed natural immunity to HBV among the subjects clinically diagnosed as having hepatitis and has become noninfectious. It also suggests that some of our subjects sero-positive for HBeAg, anti-HBe, anti-HBc and anti-HBs especially in presence of HBV DNA could be having co-infection of HBV strains of distinct genotypes [15]. This emphasizes the important role of serological assay in the assessment of the patient with HBV infection [3,17].

The detection of coinfection of HBV and HCV among only our subjects with high, medium and low infectivities is very important as it suggests a super infection with HCV favours the infectivity of HBV among Nigerians [18]. Furthermore, the high rate of HBV infectivity observed among our subjects could explain the high prevalence of hepatocellular cancer among Nigerians [15], more so there is associated increased risk of its development in the presence of HBeAg [19]. The observation that the distribution of the different statuses of HBV infectivity in our subjects is unaffected by the gender is not unexpected because the natural course of the infection is similar in both sexes. The age distribution of all the different HBV infectivities among subjects follows the reported epidemiological pattern of the infection among Nigerians [4].

In conclusion, our study shows that HBV is very infectious among Nigerians though in varying degrees with low infectivity as the commonest type and occurs both in asymptomatic subject as well as in those that present clinically while a high proportion of the population are susceptible. In addition, coinfection with HCV may augment the contagiousness of HBV infection. However, further studies will be needed to ascertain the different genotypes of both HBV and HBV that are prevalent among Nigerians.

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