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HEPATITIS B VIRUS AND HIV INFECTIONS AMONG PATIENTS IN MULAGO HOSPITAL

F.N. Nakwagala, MBChB, MMed (Int. Med.) Makerere, Medical Officer Special Grade, Mulago Hospital and M.M. Kagimu, MBChB, MMed (Int.Med), MSc (CTM), Senior Lecturer, Department of Medicine, Makerere University Medical School, P.O. Box 7062, Kampala, Uganda.

Request for reprints to: Dr. M.M. Kagimu, Department of Medicine, Makerere University Medical School, P.O Box 7062, Kampala, Uganda.

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F.N. NAKWAGALA and M.M. KAGIMU

ABSTRACT

Objective: To compare the frequency of exposure to hepatitis B infection among HIV seropositive and HIV seronegative medical outpatients.

Design: Case control study.

Setting: Mulago hospital medical outpatient clinics.

Patients: One hundred and twenty nine consecutive HIV seropositive patients and one hundred and twenty nine HIV seronegative control patients.

Results: The frequency of anti-HBc among the HIV seropositive patients was 65.1% compared to 41.9% in the HIV seronegative patients (95% confidence interval: 1.51-4.45; p-value: 0.0002). Of the 84 HIV positive patients with anti-HBc, 52 (61.9%) had more than five lifetime sexual partners. In comparison, of the 45 HIV positive patients with no anti-HBc, only 18 (40%) had more than five lifetime sexual partners (95% confidence interval: 1.04-1.80; p-value: 0.028). There was no significant difference in the frequency of HBsAg and HBeAg among the HIV seropositives and HIV seronegatives.

Conclusion: The frequency of previous exposure to hepatitis B infection was higher among HIV seropositive patients compared with HIV seronegative patients and was associated with a greater number of lifetime sexual partners. Safe sexual behaviour and reduction in the number of sexual partners should continue to be promoted in the community including HIV positive patients, because it is likely to have the added advantage of reducing coincident exposure to HBV infection. This is especially important for the immunocompromised HIV positive patients who are more likely to develop a chronic infectious carrier state and among whom HBV control by vaccination is less effective than in the immunocompetent individuals.

INTRODUCTION

Transmission of HIV infection is mostly through high risk sexual activity. HBV infection is similarly transmitted by this route. The prevalence of past exposure to HBV among HIV seropositive patients has been found to vary in different geographical areas. In the USA, 90% of HIV seropositive patients had evidence of past exposure to HBV infection(1,2). In Kenya, 78% of HIV seropositive patients had evidence of past exposure to HBV(3). In Tanzania, 62% of HIV positive patients had markers of HBV infection(4). In South Africa evidence of previous exposure to HBV was found in 41% of patients(5). This study was done to assess the HBV/HIV co-infection situation in Uganda.

MATERIALS AND METHODS

The study was conducted in Mulago hospital medical outpatient department between December 1999 and January 2000. Patients attending the HIV clinic and the general medical outpatient clinics formed the study population. Consecutive patients above 14 years of age in the HIV clinic who consented to participate in the study were recruited. These were matched for age and sex by consecutive patients recruited in general

medical outpatient clinics. All patients had pre-test counselling for the HIV test. A questionnaire was administered to each patient to collect data on demographic characteristics and possible risk factors including lifetime number of sexual partners and previous blood transfusion. A blood sample (5-8 mls) was taken from each patient to test for HIV/HBV markers.

The HIV serology test was done in the research laboratory of the Department of Medicine using the rapid Abbot Determine method of Abbot diagnostics. This is a qualitative immunoassay test for detection of antibodies to HIV-1 and HIV-2 in the serum. It is reported to have a sensitivity of 100% and specificity of 99.8%.

Markers for HBV infection were done at Nakasero blood bank using Murex Wellcozyme 3rd generation ELISA tests from Abbot diagnostics. Three markers for HBV were tested, namely: hepatitis B surface antigen (HBsAg), hepatitis B e antigen (HBeAg) and antibodies to hepatitis B core antigen (Anti-HBc). HBeAg was only done on samples with HBsAg. Data entry and analyses were done using the Epi Info 6 computer programme.

RESULTS

There were 142 patients interviewed for recruitment into the study from the HIV clinic. Five of these did not consent to enter the study. Of the remaining 137 patients, 122 were HIV seropositive and 15 HIV seronegative. Out

of the 122, eleven had no matching HIV seronegative controls and they were excluded from the study. Therefore there were a total of 111 HIV seropositive patients who were finally recruited from the HIV clinic. Of the 15 HIV seronegative patients from this clinic, 12 were recruited into the HIV seronegative group and three were excluded because they could not be matched with any HIV seropositives.

There were 209 patients from the general medical outpatient clinics who were interviewed for recruitment into the HIV seronegative control group. Of these 70 did not consent to enter the study. This left 139 patients. Of which four were later excluded because of a laboratory accident in which their blood samples were destroyed in a centrifuge. Of the remaining 135, 117 were HIV seronegative. These were recruited into the HIV seronegative control group. The remaining 18 patients who were HIV seropositive were recruited into the HIV seropositive group. This made a total of 129 patients recruited for the HIV seropositive group and the same number for the HIV seronegative group.

The age, gender, marital status, residence, ethnicity and education were similar in the two groups with no significant difference (Table 1). The proportion of Muslims was significantly higher among the HIV negative group compared to the HIV positive group (23.2% and 13.1% respectively, 95% confidence interval: 1.03-4.23; p-value: 0.037). The prevalence of anti-HBc indicating past exposure to HBV was significantly higher among HIV positive patients compared to HIV negative patients (Table 2). There was no difference in the prevalence of current infection with HBV in the two groups as measured by the prevalence of HBsAg and HBeAg. Among HIV negative patients with anti-HBc the proportion of rural residents was significantly higher compared to urban residents. In addition, the proportion of patients from the Nilotic and Nilo-hamitic ethnic groups which predominate in the northern part of Uganda was significantly higher compared to the Bantu ethnic group from the southern part of Uganda (Table 3).

Table 1

Demographic characteristics among HIV seropositive and seronegative patients

Variable	HIV positive n= 129	HIV negative (%)	CI n= 129	P (%)
<i>Age</i>				
Mean age	34.4	34.4		0.997
Age range	16-70	16-66		
<i>Marital status</i>				
Married	62 (48.1)	76 (58.9)		0.204
Separated/divorced/widowed	52 (40.2)	23 (17.7)		0.051
Never married	15 (11.6)	30 (23.2)		0.692
<i>Sex</i>				
Females	78 (60.5)	78 (60.5)		
Males	51 (39.5)	51 (39.5)	0.59-1.71	1.000
<i>Occupation</i>				
Professional	20 (15.5)	22 (17.0)		
Non-professional	109 (84.5)	107 (83.0)	0.43-1.83	0.866
<i>Residence</i>				
Urban	27 (21.1)	33 (25.6)		
Rural	102 (78.9)	96 (74.4)	0.43-1.50	0.853
<i>Ethnicity</i>				
Bantu	122 (94.6)	116 (89.6)		
Nilotic/Nilo-Hamites	7 (5.4)	13 (10.4)	0.69-5.68	0.244
<i>Education level</i>				
Non/Primary	74 (57.4)	66 (51.2)		
Secondary/Tertiary	55 (42.6)	63 (48.8)	0.76-2.17	0.421
<i>Religion</i>				
Christian	112 (86.9)	99 (76.8)		
Muslim	17 (13.1)	30 (23.2)	1.03-4.23	0.037

CI = 95% confidence interval P = p-value

Table 2

Prevalence rates of HBV markers among HIV seropositive and HIV seronegative patients

Marker	HIV positive n = 129 (%)	HIV negative n = 129 (%)	CI	P
Anti-HBc	84 (65.1)	54 (41.9)	1.51-4.45	0.0002
HBsAg	23 (17.8)	17 (13.1)	0.68-3.00	0.302
HBeAg	6 (4.7)	3 (2.3)	0.36-2.56	0.497

Table 3

Demographic characteristics for patients with past HBV infection (anti-HBc + ve)

Variable	HIV +VE			CI	P	HIV -VE			CI	P
	N ₁	n ₁	(%)			N ₂	n ₂	(%)		
Age: Less than 40	88	55	(62.5)	0.28-1.66	0.361	90	39	(43.3)	0.53-2.86	0.811
40 or more	41	29	(70.7)			39	15	(38.5)		
Education				0.33-1.65	0.478				0.33-1.54	0.348
None/primary	74	46	(62.2)			66	25	(37.9)		
Secondary/tertiary	55	38	(69.1)			63	29	(46.0)		
Marital status				0.66-3.45	0.292				0.74-3.57	0.183
Married	62	42	(67.7)			76	36	(47.4)		
Separated/divorced/ widowed	52	32	(61.5)			23	9	(39.1)		
Never married	15	10	(66.7)		0.779	30	9	(30.0)		0.253
Sex: Male	51	36	(70.6)	0.42-4.28	0.618	51	25	(49.0)	0.26-2.16	0.566
Female	78	48	(61.5)			78	29	(37.2)		
Occupation				0.64-5.25	0.272				0.13-0.92	0.017
Professional	20	14	(70.0)			22	8	(36.4)		
Non-professional	109	70	(64.2)			107	46	(43.0)		
Residence				0.56-1.47	0.962				0.37-0.-6	0.034
Urban	28	21	(75.0)			33	8	(24.2)		
Rural	101	63	(62.4)			96	46	(47.9)		
Ethnicity: Bantu	122	79	(64.8)	0.42-4.43	0.559	116	45	(38.8)	0.24-1.45	0.206
Nilotic/Nilo-Hamites	7	5	(71.4)			13	9	(69.2)		
Religion: Christian	112	74	(66.1)			98	38	(38.8)		
Muslim	17	10	(58.8)			31	16	(51.6)		

N₁ = Number of patients in each sub-group among HIV +ve patientsn₁ = Number of HIV positive patients with anti-HBc in each sub-group.N₂ = Number of patients in each sub-group among HIV negative patientsn₂ = Number of HIV negative patients with anti-HBc in each sub-group.

Table 4

Demographic characteristics for patients with current HBV infection (HBsAg + ve)

Variable	HIV +VE			CI	P	HIV -VE			CI	P
	N ₁	n ₃	(%)			N ₂	n ₄	(%)		
Age: Less than 40	88	20	(22.7)	0.98-9.86	0.033	90	13	(14.4)	0.46-5.57	0.518
40 or more	41	3	(7.3)			39	4	(10.3)		
Education				0.14-1.12	0.079				0.26-2.58	0.716
None/primary	74	9	(12.5)			66	8	(12.1)		
Secondary/tertiary	55	14	(25.5)			63	9	(14.3)		
Marital status				1.28-10.5	0.005				1.32-16.1	0.005
Married	62	12	(19.4)			76	11	(14.5)		
Separated/divorced/ widowed	52	5	(9.6)			23	3	(13.0)		
Never married	15	6	(40.0)		0.023	30	3	(10.0)		0.828
Sex: Male	51	15	(29.4)	0.46-5.40	0.552	51	12	(23.5)	0.21-4.53	0.782
Female	78	8	(10.3)			78	5	(6.4)		
Occupation				0.10-1.96	0.457				0.12-2.43	0.612
Professional	20	5	(25.0)			22	3	(13.6)		
Non professional	109	18	(16.5)			107	14	(13.1)		
Residence: Urban	28	3	(11.1)	0.08-4.24	0.798				0.04-0.79	0.016
Rural	101	20	(19.6)			96	14	(14.6)		
Ethnicity: Bantu	122	21	(17.2)			116	12	(10.3)		
Nilotic/Nilo-Hamites	7	2	(28.6)			13	5	(38.5)		
Religion: Christian	112	19	(17.0)	0.17-2.75	0.750	98	15	(15.3)	0.57-9.81	0.334
Muslim	17	4	(23.5)			31	2	(6.5)		

N₁ = Number of patients in each subgroup among HIV+ve patients
n₃ = Number of HIV positive patients with HBsAg in each subgroupN₂ = Number of patients in each subgroup among HIV negative patients.
n₄ = Number of HIV negative patients with HBsAg in each subgroup.

In both HIV positive and HIV negative patients with HBsAg, the proportion of males was significantly higher compared to females with a male/female ratio of approximately 3:1 (Table 4). From Table 4, it can be seen that among the HIV seronegative group with HBsAg, the proportion of patients from the Nilotic and Nilo-hamitic ethnic groups was significantly higher compared to the Bantu ethnic group.

Risk factors for exposure to HBV that were analysed included history of blood transfusion and lifetime number of sexual partners. A history of blood transfusion was not a significant risk factor for exposure to HBV. None of the patients with HBsAg had this history among the HIV seropositive and HIV seronegative patients. However, a higher lifetime number of sexual partners was a significant risk factor for exposure to both HIV and HBV infections. Of the 129 HIV positive patients, 70 (54.2%) had more than five lifetime sexual partners compared to 52 (40.3%) of the 129 HIV seronegative patients (95% confidence interval: 1.04-2.79; p-value: 0.034). Furthermore, among the 138 patients with anti-HBc, 78 (56.5%) had more than five lifetime sexual partners while among the 120 patients without anti-HBc, only 42 (35%) had more than five lifetime sexual partners (95% confidence interval: 1.41-4.13; p-value: 0.0008).

Among the HIV positive patients, those who had anti-HBc were more likely to report more than five lifetime sexual partners compared to those who did not have this marker. Of the 84 HIV positive patients with anti-HBc, 52 (61.9%) had more than five lifetime sexual partners. On the other hand, of the 45 HIV positive patients without anti-HBc, only 18 (40%) had more than five lifetime sexual partners (95% confidence interval: 1.04-1.80; p-value: 0.028).

DISCUSSION

The results of this study indicate that past exposure to HBV is commoner among HIV positive patients compared to HIV negative adult patients. The prevalence rate of past exposure to HBV of 65% in HIV positive patients is not very different from the rates of 62% and 78% found by others in neighbouring Tanzania and Kenya respectively(3,4). However, it differs from the rate of 41% found by South African researchers(5) and the rate of 90% in USA(1).

Patients with HBsAg were predominantly male, with a male/female ratio of 3:1. A study in Mwanza in Tanzania showed a male predominance of HBsAg carriers with a male to female ratio of 2.2:1. Among the HIV seronegative patients with HBsAg and anti-HBc, the proportion of those from the Nilotic and Nilo-hamitic ethnic groups was significantly higher compared to the Bantu ethnic group. The variation in HBV infection rates among different regions and ethnic groups was also observed in a study from South Africa(7). The explanation for this variation in Uganda needs further studies to try to identify the responsible factors.

In the HIV seronegative group there was a higher proportion of Muslims compared to Christians. A similar observation was made in Uganda while studying the incidence of HIV infection. One possible explanation given is that Muslim behaviour and practices such as circumcision may reduce HIV transmission(8).

In our study, past exposure to HBV among HIV positive patients was associated with a higher number of lifetime sexual partners in comparison with HIV positive patients without past exposure to HBV. This suggests that patients who were more sexually active had a greater chance of being exposed to both HIV and HBV. However, most of these patients were able to contain the HBV infection so that their current infection rate as evidenced by HBsAg does not differ from that of the HIV negative patients. Similar observations have been made elsewhere.

If HIV positive patients with reduced immunity are re-infected with HBV, a large proportion of them are likely to develop a chronic carrier state with highly infectious serum and body fluids in comparison with those who are HIV negative(9,10). It is therefore important to prevent exposure to HBV infection among HIV positive patients. HIV infected patients respond poorly to vaccination when compared with healthy individuals (11,12). Under these circumstances safe sex is an option that should be given priority in the prevention of exposure to HBV in HIV positive patients.

With improved management of AIDS patients, several studies have reported increases in unsafe sex in these patients (13,14). It is therefore, important to continue to emphasise to HIV positive patients that reduction in sexual partners and safe sex have the added advantage of reducing exposure to other sexually transmitted diseases including HBV.

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