HEPATITIS B AND C SEROPOSITIVITY IN A COHORT OF HIV-POSITIVE PATIENTS IN ILORIN, NORTH-CENTRAL NIGERIA

*Udeze AO[1], Ali UM[1], Adeoye PA[1], Odugbesi AE[1], Sule WF[2], Okonko IO[3]

Virology Unit, Department of Microbiology, University of llorin, P.M.B 1515 Ilorin-Nigeria

2Department of Biological Sciences, College of Science, Engineering and Technology, Osun State University, PMB 4494, Osogbo, Osun State, Nigeria

3Department of Microbiology, University of Port Harcourt, Choba, P.M.B, 5323 Port Harcourt, River State, Nigeria

Tel.: +234 (81)35586003

Abstract: Since HIV, HBV and HCV share common routes of transmission and acquisition, HIV-infected patients are likely exposed to HB and C viruses. We hypothesised that there was no difference between prevalence rate of HB and C infections among HIV-infected patients accessing healthcare at HIV and AIDS section of University of Ilorin Teaching Hospital, Ilorin, Nigeria. This is a hospital-based cross sectional study. After obtaining ethical approval, we consecutively selected consenting 356 participants from whom we obtained pertinent socio-demographic data using questionnaire forms; after which we aseptically collected blood samples and prepared plasma from each. The latter were tested, using ELISA, for presence of HBsAg and anti-HCV antibody. The results were analyzed using t-test and binary logistic regression. Of the 356 (128 males and 228 females: age range 7 months-70 years, mean age 36.5 years) HIV-infected participants, 114 (32.0%) and 14 (3.9%) were respectively positive for HBsAg and anti-HCV antibody; these respectively represented dual HIV-HBV and HIV-HCV infection rates. The HIV-positive participants had more than 11 times (p=0.001) likelihood of being HBsAg positive than being anti-HCV antibody positive. Group-specific prevalence rate was also higher for HIV-HBV dual infection. Conclusively, the HIV-infected participants had significantly higher HB rate compared to HC, this was suggestive of higher infectiousness of HBV and greater exposure to HBV than HCV. The only variable predictive of HIV-HCV or HIV-HBV dual infection was education. But, occupation and history of blood transfusion were respectively predictive of HIV-HBV and HIV-HCV dual infection among the study participants.

Key words: dual infection, hepatitis B, hepatitis C, HIV-positive, Nigeria, seropositivity

INTRODUCTION

Hepatitis C virus (HCV) and hepatitis B virus (HBV) infections were hitherto not considered a major clinical problem in HIV infected individuals. Their contributions to liver-related morbidity and mortality became significant following the introduction of Highly Active Antiretroviral Therapy (HAART) which significantly improved survival in HIV- infected patients.

*Corresponding author:
udeze.ao@unilorin.edu.ng, austok90@yahoo.com Udeze AO[1]

HIV/HCV and HIV/HBV co-infections leads to synergistic effect on disease progression as a result of which patients with the co-infection are predisposed to developing liver cirrhosis and end-stage liver disease than their mono-infected HCV-positive (HCV+) or HBV-positive (HBV+) counterparts (Qurishi *et al.*, 2003). HIV patients co-infected with HCV or HBV have higher frequency of liver toxicity associated with HAART (Saves *et al.*, 1999, Nunez *et al.*, 2001, Dieterich *et al.*, 2002, Soriano *et al.*, 2002). Co-infection of HIV-infected individuals with HCV and/or HBV are common presumably due to the shared route of transmission of these viruses (Santiago-Munoz *et al.*, 2005). Approximately 170 million people worldwide are chronically infected with HCV (Maddava *et al.*, 2002) while an estimated 320-350 million individuals are chronic carriers of HBV and about 1.5 million people die annually from HBV-related causes (Alao *et al.*, 2009). Nigeria is among the countries highly endemic for viral hepatitis (Odemuyiwa *et al.*, 2001; Inyama *et al.*, 2005) where an estimated 75% of the population is believed to have been exposed to hepatitis viruses at one time or the other in their life and that about 7% of these will die from its complications (Mutimer *et al*, 1994). Prior to the discovery of HIV/AIDS in Nigeria, enforcement of regulations guiding blood transfusion in many localities was not in existence leading to indiscriminate blood transfusion practices and the dominance of commercial donors among blood donors. Patronage of patent medicine stores or some other substandard settings for treatment of ailments where unsterilized sharps were often used was the order of the day (FMHN, 2004). The use of condoms for sexual practice was not common. These harmful practices contributed immensely to the high prevalence of these co-infections in the country. In recent years however, there has been an increased awareness on the dangers of these harmful practices with an expected decline in rate of these infections. Continued high prevalence of the co-infection therefore calls for the need to evaluate other practices that might contribute to the high endemicity. This work was therefore undertaken to determine the rate of HIV/HBV and HIV/HCV dual infections among attendees of a tertiary health facility and identify some contributory factors.

MATERIALS AND METHODS

Study design and area

This was a cross-sectional, tertiary health facility-based study conducted between May and August, 2012 at the University of Ilorin Teaching Hospital (UITH), Ilorin, Kwara State, North-central Nigeria. The study was conducted according to ethical standards for human studies and approved by Ethical Committee of the Teaching Hospital. Each study participant provided informed consent before sampling.

Subjects and Samples

Blood samples were aseptically collected from 356 (128 males and 228 females: age range 7 months - 70 years; mean age 36.5) confirmed HIV-infected individuals attending University of Ilorin Teaching Hospital. Sample size was determined using Fischer's formula (Araoye, 2003). Socio-demographic data were collected using interviewer-administered questionnaire. The data were analyzed with SPSS 15.0 for Windows and $p \leq 0.05$ was used as indicator of statistical significance. About 5ml of blood sample was aseptically collected from each participant into EDTA bottle and centrifuged to separate the plasma from packed blood cells. The plasma was aspirated into new Eppendorf tubes, appropriately labelled and stored at $-20^{o}C$ until assayed.

Serology

Samples were tested for the presence of antibodies to HCV using commercially available 3rd generation enzyme-linked immunoabsorbent assay (ELISA) (DIA PRO Diagnostic Bioprobes, Millano-Italy). The samples were also tested for the presence of hepatitis B surface antigen (HBsAg) by Monolisa Ag HBs plus ELISA (Bio Rad France) according to manufacturer's instructions.

Statistical analysis

Data generated is presented with descriptive statistics. Statistical associations or a lack thereof between participant variables and prevalence rates of dual infection were determined using binary logistic regression analysis to estimate odds ratios (OR) with 95% confidence intervals (CI) (Ho *et al.*, 1997; Pallas *et al.*, 1999). A p value of ≤0.05 was set as indicator of statistical significance. The analysis was performed with SPSS 15.0 for Windows (SPSS Inc., Chicago, IL)

RESULTS

A total of 356 ((128 males and 228 females: age range 7 months - 70 years; mean age 36.5years) HIV-infected participants were studied. Among the 356 HIV-positive persons tested for HBsAg, 114 tested positive, 242 tested negative, yielding odds of 114 /242 (0.47) for HBsAg positivity. That is, HBsAg positivity was 0.47 times as likely as was HBsAg negativity. Among same study participants tested for anti-HCV, 14 tested positive, 342 tested negative, yielding odds of 14 /342 (0.04) for anti-HCV antibody positivity. This implied that anti-HCV positivity was 0.04 times as likely as was anti-HCV negativity. The ratio of these odds (known as odds ratio [OR]) is therefore, 11.75 (p=0.001). This indicated that an HIV-positive study participant had more than 11 times likelihood of being HBsAg positive than being anti-HCV antibody positive. We observed however, that none of the study HIV-infected participants had triple infection (i.e. 0.0% HIV-HCV-HBV infection).

We recorded that 3.5% and 4.7% HIV-infected females and males were respectively positive for anti-HCV antibody; other group-specific prevalence rates are shown in Tables 1, 2 and 3. It was observed that for both tests, the females had lower prevalence rates; however, gender had no statistical association with either serologic test (Table 1).

As regards age, highest anti-HCV antibody was observed among the 21-30 years age range, while corresponding observation for HBsAg was among the 41-50 years old. Age also had no statistical association with either prevalence rate (Table 1). The 41-50 years and those aged 50 years and above had no evidence of HCV infection.

We observed that the single HIV-infected participants had higher prevalence rates for either anti-HCV antibody or HBsAg compared to the married; however, marital status had no significant influence on the prevalence rate of either serologic outcome. The widows had smallest size with zero prevalence rate for anti-HCV antibody but 14.3% for HBsAg (Table 1).

Education was observed as the only variable independently associated with anti-HCV antibody or HBsAg positivity, Table 1; while only those with no formal education had significantly higher HCV antibody prevalence rate compare to those with secondary education; the situation was different for HBsAg, those with no formal education had significantly higher HBsAg prevalence rate compare to those with primary education. It is noteworthy however; that those HIV-infected participants without formal education had highest prevalence rates for either anti-HCV antibody or HBsAg.

Occupation of participants had no association with prevalence of anti-HCV antibody but, it did for HBsAg with students having about 5 times more likelihood of being HBsAg positive compared to the unemployed (Table 2).

The HIV-infected participants with history of receipt of blood transfusion had significantly higher anti-HCV antibody prevalence rate compared to those who reported "no" (Table 3).

There was no association between history of blood transfusion and HBsAg positivity; the same for scarification and circumcision for either anti-HCV antibody or HBsAg prevalence rate.

Table 1: Socio-demographic factors and their association with serologic outcomes among HIV-infected participants in University of Ilorin Teaching Hospital, North-Central Nigeria

Factors	No tested	HCV			HBV		
		No positive (%)	Odds ratio (95% confidence interval)	P Value	No positive (%)	Odds ratio (95% confidence interval)	P Value
Gender							
Female	228	8 (3.5)	1a		69(30.3)	1a	
Male	128	6 (4.7)	1.352(0.46-3.99)	0.584	45(35.2)	1.249(0.79-1.98	0.343
Age (yrs)							
≤ 20	40	6 (15)	2.851E8	0.997	12(30)	1.041(0.42-2.61)	0.932
21-30	74	4 (5.4)	9.231E7	0.997	24(32.4)	1.166(0.53-2.57)	0.704
31-40	114	4 (3.5)	5.874E7	0.998	36(31.6)	1.121(0.54-2.34)	0.762
41-50	80	0 (0)	1.000	1.000	28(35)	1.308(0.60-2.83)	0.497
> 50	48	0 (0)	1a		14(29.2)	1a	
M S							
Single	76	8 (10.5)	1.901E8	0.99	30(39.5)	3.913(0.82-18.73)	0.088
Married	266	6 (2.3)	3.728E7	0.99	82(30.8)	2.674(0.59-12.22)	0.205
Widowed	14	0 (0)	1a		2(14.3)	1a	
Ed							
No	44	4 (9.1)	5.700(1.01-32.32)	0.049*	20(45.5)	5.139(2.19-12.04)	0.001*
Primary	86	6 (7.0)	4.275(0.84-21.72)	0.08	12(14.0)	1a	
Secondary	116	2 (1.7)	1a		46(39.7)	4.052(1.98-8.28)	0.001*
Tertiary	110	2 (1.8)	1.056(0.15-7.63)	0.957	36(32.7)	3.000(1.45-6.22)	0.003*

1a = reference group

*=significant association

No= number, MS= marital status, Ed= education

Table 2: Occupation and its association with serologic outcomes among HIV-infected participants in University of Ilorin Teaching Hospital, North-Central Nigeria

Occupation	No tested	HCV			HBV		
		No positive (%)	Odds ratio (95% confidence interval)	P Value	No positive (%)	Odds ratio (95% confidence interval)	P Value
Civil servants	52	2 (3.9)	6.462E7	0.99	22 (42.3)	4.400(0.89-21.68)	0.069
Students	30	2 (6.7)	1.154E8	0.99	14 (46.7)	5.250(0.99-27.61)	0.05*
Farmers	12	2 (16.7)	3.231E8	0.99	0 (0)	0.000	0.99
Artisans	62	0 (0)	1.000	1.00	14 (22.6)	1.750(0.35-8.76)	0.496
Traders	152	4 (2.6)	4.366E7	0.99	46 (30.3)	2.604(0.56-12.10)	0.222
HWs	4	0 (0)	1.000	1.00	4 (100)	9.693E9	0.99
Military	6	2 (33.3)	8.077E8	0.99	2 (33.3)	3.000(0.31-28.84)	0.341
Drivers	8	0 (0)	1.000	1.00	4 (50.0)	6.000(0.78-46.13)	0.085
Dependants	16	2 (12.5)	2.308E8	0.99	6 (37.5)	3.600(0.59-21.93)	0.165
Unemployed	14	0 (0)	1a		2 (14.3)	1a	

1a = reference group

*=significant association

No= number, HWs= health workers

Table 3: Some risk factors of transmission and their association with serologic outcomes among HIV-infected participants in University of Ilorin Teaching Hospital, North-Central Nigeria

Factors	No tested	HCV			HBV		
		No positive (%)	Odds ratio (95% confidence interval)	P Value	No positive (%)	Odds ratio (95% confidence interval)	P Value
HBT							
Yes	94	8 (8.5)	3.969(1.34-11.76)	0.013*	26(27.7)	1[a]	
No	262	6 (2.3)	1[a]		88(33.6)	1.323(0.79-2.22)	0.291
Sc							
Yes	140	0 (0)	1[a]		50(35.7)	1.319(0.84-2.08)	0.230
No	216	14 (6.5)	1.120E8	0.99	64(29.6)	1[a]	
Cir							
Yes	172	6 (3.5)	1[a]		54(31.4)	1[a]	
No	184	8 (4.3)	1.258(0.43-3.70)	0.677	60(32.6)	1.057(0.68-1.65)	

1[a] = reference group
*=significant association
No= number, HBT= history of blood transfusion, Sc= scarification, Cir= circumcision

Discussion

This work was undertaken to determine the rate of HIV-HBV and HIV-HCV dual infections among attendees of a tertiary health facility with the view to identifying some contributory factors. Our study shows that 32.0% of the 356 HIV-patients studied were HBsAg positive, while 3.9% were positive for anti-HCV antibodies. These, together with the observation that the study HIV-infected individuals were 11 times more likely to be infected with HBV than HCV further demonstrates endemicity of Nigeria for HBV as previously reported (Olatunji and Iseniyi, 2008).

As the study participants were all HIV-positive, it implied that HIV-HBV dual infection rate was 32.0%; this is quite considerable and shows that HBV infection still remains a threat to HIV patients in this region of the country. This result is comparable with earlier reports (Stud *et al.*, 2001; Olatunji and Iseniyi, 2008); but Lower prevalence rates of 9.7% (Sirisena *et al.*, 2002) 14.8% (Agbaji *et al.*, 2005); 25.9% (Uneke *et al.*, 2005) and 20.6% (Forbi *et al.*, 2007) of HIV-HBV dual infection had earlier been reported from Jos, the same North-central Nigeria. The 32.0% HIV-HBV prevalence rate recorded in this study signifies that the situation, rather than abating, is on the increase. Higher prevalence rate than ours was however, reported in Kano, northern Nigeria (Nwokedi *et al.*, 2006). Elsewhere in the world, lower prevalence rates have equally been reported; 4.8% in Australia (Petoumenos and Ringland, 2005), 6% in Nairobi, Kenya (Harania *et al.*, 2008), 4.47% in New York city USA (Kim *et al.*, 2008), 25.5% in Slovenia (Seme *et al.*, 2009), 13% in Ghana (Sagoe *et al.*, 2012).

Our result also shows higher prevalence of HIV/HBV dual infection among the males than the females, although the difference was not significant (Table 1). Similar pattern have also been reported in Ibadan South-western Nigeria and several reasons suggested which include; boys' predilection for aggressive sports and plays that may result in injury with bleeding, societal acceptance of multiple sexual partners for men than women (Otegbayo *et al.*, 2008). Other likely reason is the mandatory circumcision of the males, a practice that has been discontinued in the females (Udeze *et al.*, 2012).

The prevalence rate of HIV-HCV dual infection among the study HIV-positive patients of 3.9% was comparable with a result in Ghana (Sagoe *et al.*, 2012). This rate, 3.9% is relatively high compared to prevalence rate of 2.3% in Abuja, Nigeria (Adewole *et al.*, 2009) and 1.0% in Kenya (Harania *et al.*, 2008). Higher prevalence rate of HIV-HCV dual infection had been reported from other countries. From USA/Europe, Verucci *et al.* (2004) reported a prevalence of 35%. In 1998, Stubbe *et al.* reported a 33.0% HCV dual infection with HIV from the EuroSIDA study. The study also showed that 75% of injection drug users (IDUs) in the population were co-infected. Similarly, Hershow *et al* (1997) showed a 33.0% prevalence of HCV RNA among HIV-positive pregnant women in the United States. From Brazil, Segurado *et al* (2004) reported a prevalence of 36.2%. The relatively low prevalence rate of HIV-HCV dual infection obtained in our study compared to the figures from the more developed countries could be as a result of low level of indulgence of Nigerians in intravenous drug use (IDU), a veritable risk factor for transmission of HIV, HBV and HCV (CDC, 1998; Lowe and Cotton, 1999; Maier and Wu, 2002; Aceijas and Rhodes, 2007).

The rate of HIV-HCV dual infection appeared to decline with advancing age starting with 15% in the age group of ≤ 20 years to 0.0% in the age > 50 years while somewhat steady rate was observed for all age groups for HIV-HBV dual infection. Analysis of age as a variable however showed no association with both HIV-HBV and HIV-HCV dual infections (Table 1). This is slightly different from a similar study carried out in North-eastern Nigeria in which age group 10-19 years had the highest prevalence of HIV-HBV dual infection with age group 40-49 years having the highest dual infection of HIV-HCV (Denue *et al.*, 2012). Also, in another study conducted in Jos, highest prevalence of HIV-HBV dual infection was recorded among age group 51-60 years (Uneke *et al.*, 2005). The reason for this difference in age distribution was not immediately apparent to us.

With regard to marital status of the participants, highest prevalence of 10.5% and 39.5% were observed for HIV-HCV and HIV-HBV dual infections respectively among single patients; while the lowest prevalence of 0.0% and 14.3% were observed for HIV-HCV and HIV-HBV dual infections respectively among the widowed patients. Analysis of the results however, showed no association of marital status with the dual infections (Table 1). Highest dual infection rate of both HIV-HBV and HIV-HCV observed among the singles might not be unconnected with the fact that this group of people are more likely to have multiple sexual partners and engage in unprotected sexual intercourse.

Analysis of the interaction of educational status and the dual infections showed that lack of formal education was independently associated with both dual infections. The significantly higher rates of both HIV-HCV and HIV-HBV dual infections observed among participants without formal education is not unexpected since lack of formal education is synonymous with lack of awareness; thus engage in such behaviours and practices that expose them to both HBV and HCV.

With regard to occupational status of the participants, highest HIV-HCV dual infection rate of 33.3% was recorded among military personnel. Artisans, health workers, drivers and unemployed people all have zero prevalence of the dual infection. Analysis of the result showed no significant statistical association with HIV-HCV dual infection. Concerning HIV-HBV dual infection, highest prevalence rate of

100% was recorded among health workers suggesting that healthcare settings still play a role in the transmission of HBV in our society as previously reported (Olubuyide *et al.*, 1997). However, strong association was observed between being a student and having HIV-HBV dual infection (Table 2).

Having history of blood transfusion showed a strong association (p=0.013) with HIV-HCV dual infection compared to no history of blood transfusion (Table 3). On the other hand, history of blood transfusion was not associated with HIV-HBV dual infection (Table 3). Routine screening for HBV before blood transfusion is widely practiced in most of our hospitals while HCV screening is yet to attain the same status. This might partly explain the strong association between history of blood transfusion and HIV-HCV dual infection contrary to HIV-HBV infection.

Analysis of our result also showed 6.5% prevalence rate of HIV-HCV dual infection among participants with no scarification and 0.0% among participants who had scarification. This somewhat weird observation indicated that the study HIV-infected participants were probably exposed to HCV via routes other than piercing or scarification. On the other hand, 35.7% prevalence rate of HIV-HBV dual infection was recorded among participants with scarification compared to 29.6% among participants with no scarification. The differences were however statistically insignificant (Table 3). Similarly, analysis of circumcision revealed no association of this variable with HIV-HCV dual infection, as well as, HIV-HBV dual infection (Table 3).

In conclusion, the study HIV-participants had clear evidence of greater exposure to HBV than HCV; variable predictive of both HIV-HCV and HIV-HBV dual infections was education. However, occupation and history of blood transfusion were respectively predictive of HIV-HBV and HIV-HCV dual infection among the study participants. Screening of HIV infected people for HBV and HCV is therefore advocated to guide anti-retroviral treatment options among HIV- infected individuals. Continued enlightenment of the general public and blood screening before transfusion are also recommended.

Acknowledgements

The authors would like to thank all the study subjects who consented to be part of this study. They also acknowledge Professor A.K. Salami for his close supervision during the course of the study.

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