

East African Medical Journal Vol. 93 No. 6 June 2016

PREVALENCE OF HEPATITIS B VIRUS INFECTIONS AMONG HIV INFECTED INDIVIDUALS IN NAIROBI, KENYA
S. N. Mabeya, Dip, HND, BSc, C. Ngugi, BSc, MSc, PhD, Lecturer, Department of Medical Microbiology, Jomo Kenyatta University of Agriculture and Technology, Nairobi, Kenya, A. K. Nyamache, BSc, MSc, PhD, Senior Lecturer, Department of Microbiology, Kenyatta University, Nairobi, Kenya and R. Lihana, BSc, MSc, PhD, Senior Researcher, Scientist, Centre for Virus Research, Kenya Medical Research Institute, P. O. BOX 54840, Nairobi, Kenya

PREVALENCE OF HEPATITIS B VIRUS INFECTIONS AMONG HIV INFECTED INDIVIDUALS IN NAIROBI, KENYA

S. N. MABEYA, C. NGUGI, A. K. NYAMACHE and R. LIHANA

ABSTRACT

Objectives: To determine the prevalence and characteristics of HBV infections among HIV infected individuals in Nairobi, Kenya

Design: A cross-sectional study.

Setting: Kenya Medical Research Institute HBV Laboratory, Nairobi, Kenya

Subjects: A total of four hundred HIV infected patients randomised from a Nairobi HIV comprehensive care centre between June and October 2015.

Results: Of the 400 subjects screened; (27.75%) had HBV immunisation, (3%) had acute disease, (4.75%) were on recovery, (2.5%) were in chronic stage, (1.75%) were asymptomatic and (2.25%) had occult HBV. Statistical analysis showed that age and gender were not significantly associated with the risk of HBV or occult HBV infections.

Conclusion: HIV/HBV co-infections is still >5.5% but the rates could be higher than reported here. Utility of HBV sero-markers especially in infection staging is therefore very important in disease diagnosis and surveillance.

INTRODUCTION

Human immunodeficiency virus (HIV) and Hepatitis B virus (HBV) infections are the two most important infectious diseases throughout the world particularly in developing countries (1). These viruses often share routes of transmission (perinatal, sexual and parenteral) with high cases being reported among high risk populations (1,2). In sub-Saharan Africa, it is estimated that 8–20% of HIV infected individuals are co-infected with hepatitis B virus (HBV) (2,3). Therefore in this region, most individuals are often infected at early childhood (due to close contact with household members) or in the perinatal period (from mother to baby at birth). In addition, between 70–90% of individuals in this region have previously been exposed to or are chronic carriers of HBV (4). These rates are high compared to low endemicity areas, such as in western countries, where most transmission occurs during adolescence and young adulthood due to high risk behaviours like unprotected sexual contact and injection drug use (5).

With the up scaling of ART among HIV infected individuals, its impact on surviving patients has revealed chronic liver disease from viral hepatitis B or C as a leading cause of morbidity and mortality (7). HIV accelerates the progression of liver disease in HIV/HBV co-infection (6) with patients showing an increased risk of hepatotoxicity of anti-retroviral drugs (7). Despite these concerns, the burden of HIV/HBV co-infection among Kenyans has not been fully

characterised. Although important information could be gained from studying HBV virological markers, such as hepatitis (HBeAg, HBsAg, HBVcAb and HBV-IgM) status, this information is missing from published Kenyan cohorts. This study was therefore carried out to determine the prevalence and infection stages of HBV infection in HIV cohort.

MATERIALS AND METHODS

Study population: HIV infected patients seeking treatment at Mama Lucy Hospital comprehensive health clinic in Nairobi, were considered for recruitment after giving consent. Patients who were drug naive and those who declined to consent were excluded from the study. However, those who consented were consecutively sampled and a structured questionnaire was administered. This demographic data were obtained during the study period between September and October 2015.

Five (5) millilitres of blood was collected from each participant and screened for AntiHBs, AntiHBc, AntiHBe, HBsAg and HBe sero-status using Lumiquick HBV 5 panel kit (LumiQuick Diagnostics, Inc. California, USA), according to manufacturer's instructions. Ethical clearance was obtained from Kenyatta University/National Ethical Review committee.

Data analysis: All generated data was entered into a database, cleaned and analysed using SPSS version

20. The sero-prevalence for HBV was expressed in percentages for the entire study group. Simple linear correlation analysis was used to determine the association with age, gender and HBV infection or occult hepatitis infections.

RESULTS

A total of four hundred (400) patients consisting of 293 (73.25%) female and 107 (26.75%) males were enrolled into this study. The mean age was 33.4 with females averaging 34.1 years and 31.7 years for males. Majority of the recruited participants were on first-line treatment for HIV 390 (97.5%) with only 2.5% (10) on second-line (Table 1). Those who were at acute HBV disease were 12 (3%), those at recovery 19 (4.75%) while those at chronic stage were 10 (2.5%).

However, those found immunised were 111 (27.75%), asymptomatic 7 (1.75%) and occult were 9 (2.25%) (Table 2). Majority of the co-infected patients were those aged between 3 and 49 years of age.

Of the 400 subjects under study, those detected to be infected were found to be at different stages of HBV infection (Table 2). Approximately, (27.75%) were found to have been vaccinated, those on acute phase were 3%, on recovery were 4.75%, chronic 2.5%, asymptomatic or inactive 1.75% while those on occult HBV were 2.25%

Age or gender had no significant influence that led to HBV infections. In Pearson correlation analysis, infection with HBV was found to increase with age $r=0.054$; $p=0.283$ while gender was not found to be a risk factor to infection even though males were the most affected $r=-0.62$; $p=0.213$.

Table 1

Demographic characteristic of the study participants visiting HIV care clinics of Mama Lucy Hospital, Kayole

| Gender | All N (400) | Females n(293) | Males n(107) | P-value |
|--|-------------|-------------------|-----------------|------------|
| Mean Age in years | 33.4 ± 0.01 | 34.1 ± 0.49 | 31.7 ± 2.89 | |
| HIV Mean Viral load (log10 copies/ ml) | | 8,866.52 | 9,806.55 | 7,072.9 |
| Mean Duration of treatment (years) | | 4.75 ± 0.02 | 4.6 ± 0.23 | 5.1 ± 0.12 |
| Regimen | | | | |
| AZT/3TC/NVP | 209 | 162 | 47 | |
| TDF/3TC/EFV | 168 | 112 | 57 | |
| TDF/3TC/LPr | 13 | 11 | 2 | |
| AZT/3TC/LPr | 9 | 8 | 1 | |
| Age categories (Age (years)) | | | | |
| >10 | 48 | 0.429 | | |
| 11-19. | 41 | | | |
| 20-29 | 29 | | | |
| 30-39 | 110 | | | |
| 40-49 | 104 | | | |
| 50-59 | 50 | | | |
| 60-69 | 9 | | | |
| 70-79 | 9 | | | |

KEY:

AZT: Zidovudine

3TC: Lamivudine

NVP: Nevirapine

TDF: Tenofovir Disoproxil Fumerate

LPV/r: Lopinavir/Ritonavir

Table 2

Hepatitis B virus sero-reactivities, infection stages among HIV infected individuals visiting HIV care clinics of Mama Lucy Hospital, Kayole

| sero-logical test | HBV immunisation | Acute HBV | HBV recovery | HBV chronic | inactive or asymptomatic carrier | occult HBV |
|----------------------|------------------|-----------|--------------|-------------|----------------------------------|------------|
| antiHBs | + | - | + | - | - | - |
| AntiHBc | - | + | + | + | + | + |
| AntiHBe | - | - | + | - | + | - |
| HBsAg | - | + | - | - | + | - |
| HBeAg | - | + | - | - | - | - |
| n= (400) | 111 | 12 | 19 | 10 | 7 | 9 |
| Prevalence Rates (%) | 27.75 | 3 | 4.75 | 2.5 | 1.75 | 2.25 |

DISCUSSION

In this study, we determined the prevalence of HBV among HIV infected patients seeking health service at Mama Lucy Hospital, Nairobi, Kenya. From the findings, the prevalence of HBV/HIV co-infections (5.5%) was found to be consistent with those previous obtained in Kenya, 6% (2), 5% (9), and elsewhere in Malawi (5.7%) (10,11), Nigeria (4.8%) (12) and Rwanda (4.9%) (13). However, they were also found to be higher than those obtained from regions in the country 1.1% (14) 0.7% (15), and those from Zambia (2.2%) (16), Cote d'ivoire (1.2%) (17), Gambia (0.6%) (18), Senegal (1.6%) (19) 1.8% (20) Uganda (0.6%) and Zimbabwe (0.8%) (21)

In comparison to other populations, the rates of HBV/HIV co-infection were varied. This findings ere similar to those that have been detected in other studies 4.7% (22) and elsewhere in Ethiopia 3.9% (23,24), S. Africa 4.8% (25, 26) and Uganda 4.9% (13). However, these results were also found to be low compared to those previous obtained in Kenya 55.8% (22,27) and other sub-Saharan countries; Tanzania (11,28,29), Zambia (31), Botswana (30), Malawi (11), Nigeria (12,30-33), Ethiopia (6), Argentina (34) South Africa (11,35).

Nevertheless, our findings were also found to be higher than some studies conducted in Ethiopia (25), South Africa (25,26), Uganda and Rwanda (13). The observed varied rates were associated with diverse populations, sample size as well as the methods used. The observed increase in HIV/HBV co-infection rates could be associated with an increase in access to free antiretroviral therapy that leads to prolonged life period and diverse study subjects (2). From these observation rates for general population, it shows that HBV/HIV co-infections could be higher than expected especially for high risk populations (2,36). The HIV-co-infections rates based on gender, were found to be significantly higher among male

patients compared to their female counterparts. This could be associated with the risk of infection due to their sexual behaviour with multiple partners, drug use or alcohol consumption (24). Confirmation of HBV infection in most situations has been relied upon for screening HBsAg. However, the single use HBsAg as marker for infection is insufficient for categorising patients according to various HBV infection stages of the disease or status. This limitation, has led to most people going undiagnosed which poses a challenge in disease detection and monitoring.

Despite 5 panel HBV (HBsAg, HBsAb, HBeAg, HBeAb and HBcAb) being the key for guiding in accurate diagnosis and infection staging of hepatitis B virus, only HBsAg status is often used hence risking missing detection of occult hepatitis (1,37). To our knowledge, this is the second study to apply this utility tool for HBV geno-typing and infection staging. The high recorded rates of vaccine respondents and resolved infections cases could be associated with low viral loads hence high CD4 counts among the participants. These findings concur with previously conducted studies in Kenya and elsewhere (1, 38, 39).

In the observed rates of asymptomatic carrier and occult Hepatitis, the findings were slightly higher but low among those at chronic stages compared to those previously obtained in Kenya (1,40-42). Those detected to be at chronic stage of infection, could be experiencing liver cirrhosis and therefore risking developing hepato-cellular carcinoma (2). From utility of the five HBV sero-markers, this study shows that there could be a possibility of accumulative high rates of HIV/HBV co-infections which could be at different stages of the disease (1).

This study had limitations. The study utilised IgM in classifying some of the infection stages like acute and chronic infections which could persist for several years. Secondly, this study did not determine HBV viral load and CD4/CD8 counts that could have

guided immune response and confirmation of occult HBV. In addition, this study utilised rapid serological tests which are often associated with low sensitivity and specificity in their application (1,43). Nevertheless, the utility of 5 HBV panel has demonstrated the utilisation of this technique in HBV infection response.

In conclusion, the prevalence of HBV is still remains low in the general population but this rate could be high in high risk populations. In addition, this study also confirms that HBV 5 panel sero-marker test is an important tool in guiding infection staging and geno-typing of HBV infections and therefore faster implementation of intervention measures.

ACKNOWLEDGEMENTS

To the study participants for their participation. We thank KEMRI and Mama Lucy Hospital for allowing us to conduct this study in their institutions. We appreciate JiCA-Africa and Jomo Kenyatta University of Agriculture and technology for funding this study.

REFERENCES

- Kilongosi, M. V. Budambula, R. Lihana, *et al.* Hepatitis B virus sero-profiles and genotypes in HIV-1 infected and uninfected injection and Non-injection drug users from coastal Kenya. *BMC Infect Dis* 2015; **15**: 299.
- Muriuki B. M, Gicheru M. M., Wachira, D., *et al.* Prevalence of hepatitis B and C viral co-infections among HIV-1 infected individuals in Nairobi, Kenya. *BMC Res notes* 2013; **6**:363 doi:10.1186/1756-0500-6-363
- Summer L. D, Katherine O.D, Kishorchandra N. M., *et al.* Prevalence, Clinical and Virologic Outcomes of Hepatitis B Virus Co-Infection in HIV-1 Positive Kenyan Women on Antiretroviral Therapy. *PLoS ONE*. 2013; **8**(3): e59346. doi:10.1371/journal.pone.0059346.
- Hoffmann, C. J. and Thio, C. L. Clinical implications of HIV and hepatitis B co-infection in Asia and Africa. *Lancet Infect Dis*. 2007; **7**: 402–409.
- Levanchy D. Hepatitis B virus epidemiology, disease burden, treatment, and current and emerging prevention and control measures. *J Viral Hepat*. 2004; **11**: 97–107.
- Hoffmann CJ, Charalambous S, Martin DJ *et al.*, Hepatitis B virus infection and response to antiretroviral therapy (ART) in a South African ART program. *Clin Infect Dis*. 2008; **47**: 1479–1485.
- Matthews PC, Geretti AM, Goulder PJ, *et al.*: Epidemiology and impact of HIV co-infection with hepatitis B and hepatitis C viruses in Sub-Saharan Africa. *J Clin Virol*. 2014; **61**: 20-33.
- Idoko J, Meloni S, Muazu M *et al.*: Impact of hepatitis B virus infection on human immunodeficiency virus response to antiretroviral therapy in Nigeria. *Clin Infect Dis*. 2009; **49**: 1268–1273.
- Chepkurui L, Gura Z Odhiambo F, *et al.*: Hepatitis B seroprevalence among HIV infected individuals seeking care at selected hospitals in Kericho County, Kenya, 2014. *Prim J. of Soci Sci*. 2015; **4**: 1135-1139.
- Moore E, Beadsworth MB, Chaponda M, *et al.*: Favourable one-year ART outcomes in adult Malawians with hepatitis B and C co-infection. *J Infect*. 2010, **61**: 155–163.
- Nyirenda M, Beadsworth MB, Stephany P, *et al.*: Prevalence of infection with hepatitis B and C virus and co-infection with HIV in medical inpatients in Malawi. *J Infect*. 2008, **57**: 72–77.
- Otegbayo JA, Taiwo BO, Akingbola TS, *et al.*: Prevalence of hepatitis B and C seropositivity in a Nigerian cohort of HIV-infected patients. *Ann Hepatol*. 2008, **7**: 152–156.
- Pirillo MF, Bassani L, Germinario EA, *et al.*: Seroprevalence of hepatitis B and C viruses among HIV-infected pregnant women in Uganda and Rwanda. *J Med Virol*. 2007; **79**: 1797–1801.
- Harania R, Karuru J, Nelson M, *et al.*: HIV, hepatitis B and C co-infection in Kenya. *AIDS*. 2008; **22**: 1221–1222.
- Kerubo G., Khamadi SA, Okoth V, *et al.*: Hepatitis B, Hepatitis C and HIV co-infections in two informal urban settlements in Nairobi, Kenya. *PLoS ONE* 10. 2015; (6): e012927. Doi:10.1371/journal.pone.012947
- Kapembwa KC, Goldman JD, Lakhi S, *et al.*: HIV, hepatitis B, and hepatitis C in Zambia. *J Global Infect Dis*. 2011; **3**: 269–274.
- Rouet F, Chaix ML, Inwoley A, *et al.*: HBV and HCV prevalence and viraemia in HIV-positive and HIV-negative pregnant women in Abidjan, Cote d'Ivoire: The ANRS 1236 study. *J Med Virol*. 2004, **74**: 34–40.
- Mboto CI, Fielder M, Davies-Russell A, *et al.*: Hepatitis C virus prevalence and serotypes associated with HIV in The Gambia. *Br J Biomed Sci*. 2010, **67**: 140–144.
- Diop-Ndiaye H, Toure-Kane C, Etard JF, *et al.*: Hepatitis B, C seroprevalence and delta viruses in HIV-1 Senegalese patients at HAART initiation (retrospective study). *J Med Virol*. 2008, **80**: 1332–1336.
- Enzouki AN, Elgamay SM, Zorgani A, *et al.*: Hepatitis B and C status among health care workers in the five main hospitals in eastern Libya *Infect Public Health*. 2014; **7**: 534-41.
- Kallestrup P, Zinyama R, Gomo E, *et al.*: Low prevalence of hepatitis C virus antibodies in HIV-endemic area of Zimbabwe support sexual transmission as the major route of HIV transmission in Africa. *AIDS*. 2003, **17**: 1400–1402.
- Otedo A: HBV co-infection at Kisumu district hospital, Kenya. *East Afr. Med. J*. 2004, **81**: 626–630.
- Shimelis T, Torben W, Medhin G, *et al.*: Hepatitis B virus infection among people attending the voluntary counselling and testing centre and anti-retroviral therapy clinic of St Paul's General Specialised Hospital, Addis Ababa, Ethiopia. *Sex Transm Infect*. 2008, **84**: 37–41.
- Tessema B, Yismaw G, Kassu A, *et al.*: Seroprevalence of HIV, HBV, HCV and syphilis infections among blood donors at Gondar University Teaching Hospital, Northwest Ethiopia: declining trends over a period of five years. *BMC Infect Dis* 2010, **10**: 111.
- Di Bisceglie AM, Maskew M, Schulze D, *et al.*: HIV-HBV co-infection among South African patients receiving antiretroviral therapy. *Antivir Ther*. 2010, **15**(3 Pt B): 499–503. 45
- Firnhaber C, Reyneke A, Schulze D, *et al.*: The prevalence of hepatitis B co-infection in a South African urban government HIV clinic. *S Afr Med J*.

- 2008, **98**: 541–544.
27. Okoth F, Muthia J, Gatheru Z, *et al.*: Seroprevalence of hepatitis B markers in pregnant women in Kenya. *East Afr Med J*. 2006, **83**: 485–493.
28. Wester CW, Bussmann H, Moyo S, *et al.*: Serological evidence of HIV-associated infection among HIV-1-infected adults in Botswana. *Clin Infect Dis*. 2006, **43**: 1612–1615.
29. Telatela S, Mecky MA, Munubhi E: Seroprevalence of hepatitis B and C viral co-infections among children infected with human immunodeficiency virus attending the paediatric HIV care and treatment center at Muhimbili National Hospital in Dar-es-Salaam, Tanzania. *BMC Publ Health*. 2007, **7**: 338–340.
30. Ampofo W, Nii-Trebi N, Ansah J *et al.*: Prevalence of Bloodborne Infectious Diseases in blood donors in Ghana. *J Clin. Microbi*. 2002, **40**: 3523–3525.
31. Kasolo F, Sakala I, Baboo K: Hepatitis B virus infection in human immunodeficiency virus seropositive patients at the University Teaching Hospital, Lusaka, Zambia: Interrelationship. (Abstract no. 963). 2nd IAS. Paris, France: Conference on HIV Pathogenesis and Treatment; 2003.
32. Mustapha S and Jibrin Y. The prevalence of hepatitis B surface antigenaemia in patients with Human Immunodeficiency virus (HIV) infection in Gombe, Nigeria. *Ann. Afri. Med. J*. 2004, **3**: 10–12.
33. Sud A, Singh J, Dhiman RK, *et al.*: Hepatitis B virus co-infection in HIV infected patients. *Trop Gastroenterol*. 2001, **22**: 90–92.
34. Oshitani H, Kasolo FC, Mpabalwani M, *et al.*: Prevalence of hepatitis B antigens in human immunodeficiency virus type 1 seropositive and seronegative pregnant women in Zambia. *Trans R Soc Trop Med Hyg*. 1996, **90**: 235–236
35. Lukhwani A, Burnett RJ, Selabe SG, *et al.*: Increased detection of HBVDNA in HBsAg-positive and HBsAg-negative South African HIV/AIDS patients enrolling for highly active antiretroviral therapy at a Tertiary Hospital. *J Med Virol*. 2009, **81**: 406–412.
36. Kibaya R. M, Lihana R. W. L, Kiptoo M, *et al.*: Characterization of HBV Among HBV/HIV-1 Co-Infected Injecting Drug Users from Mombasa, Kenya. *Curr HIV Resea*. 2015; **13**:4; 292-299:
37. Nagu T, Bakari M, Matee M: Hepatitis A, B and C viral co-infections among HIV-infected adults presenting for care and treatment at Muhimbili National Hospital in Dar es Salaam, Tanzania. *BMC Publ Health*. 2008, **8**:416.
38. Shafer KP, Hahn JA, Lum PJ, *et al.*: Prevalence and correlates of HIV infection among young injection drug users in San Francisco. *J Acquir Immune Defic Syndr*. 2002; **31**(4):422–431.
39. Khodadoostan M, Ataei B, Shavakhi A, *et al.*: The assessment of hepatitis B seroprevalence in persons with intravenous drug use history in the Isfahan province: Community-based study. *J Res Med Sci*. 2014; **19**(1):65–68.
40. Barth RE, Huijgen Q, Taljaard J, *et al.*, Hepatitis B/C and HIV in sub-Saharan Africa: an association between highly prevalent infectious diseases. A systematic review and meta-analysis. *Int J Infect Dis* 2010; **14**: e1024–e1031.
41. Kim NH, Scott J, Cent A, *et al.*: (2011) HBV lamivudine resistance among hepatitis B and HIV coinfecting patients starting lamivudine, stavudine, and nevirapine in Kenya. *J Viral Hepat* 2011; **18**: 447–452.
42. Day SL, Odem-Davis K, Mandaliya KN, *et al.*: Prevalence, Clinical and Virologic Outcomes of Hepatitis B Virus Co-Infection in HIV-1 Positive Kenyan Women on Antiretroviral Therapy. *PLoS ONE* 2013; **8**(3): e59346. doi:10.1371/journal.pone.0059346.
43. Njai HF, Shimakawa Y, Sanneh B, *et al.*: Validation of rapid point-of-care (POC) tests for detection of hepatitis B surface antigen in field and laboratory settings in the Gambia, Western Africa. *J Clin Microbiol*. 2015; **53**(4):1156–1163.