Texila International Journal of Public Health
Volume 7, Issue 1, Mar 2019

Sero-Prevalence and Risk Factors for HDV Infection Among HIV/HBV Co-Infected Patients in Sokoto North Western Nigeria

Article by Abdulmumini Yakubu[1], Bello Hali[2]
[1]*Department of Internal Medicine, Faculty of Clinical Sciences, College of Health Sciences, Usmanu Danfodiyo University Sokoto, Nigeria*
[2] *Department of Medical Microbiology and Parasitology, Faculty of Basic Clinical Sciences, College of Health Sciences, Usmanu Danfodiyo University Sokoto, Nigeria*
Email: yakubuabdulmumini@gmail.com[1], *yakubuabdulmumini@gmail.com*

Abstract

Background: *Hepatitis D virus infection may worsen HBV infection and about 5 % of HBV infected individuals may be infected with HDV infection as these viruses have similar routes of transmission. Severity of HBV infection is worsen by HIV co-infection. Therefore, this study aimed at the determination of prevalence and risk factors of HDV infection among HIV/HBV Co-infected individuals.*

Methods: *This was cross sectional study in which treatment-naïve HIV infected study participants were screened for HBs Ag. Study participants that were positive for HBs Ag were further screened for anti HDV and HBe Ag and also, they were assessed for $CD4^+$ T lymphocytes count, ALT and AST levels. SPSS version 20 was used for the statistical analysis and level of significance was considered at $p \leq 0.05$.*

Results: *About 4(10.8 %) of 37 HIV/HBV co-infected study were positive for anti HDV. There was no statistical association of HDV infection with different tested variables, though numerically higher among females ($P \leq 0.587$), 41-50 years age group ($P \leq 0.671$), subjects with history of multiple sexual partners ($P \leq 0.557$), blood transfusion ($p \leq 0.298$) and needle sharing ($P \leq 0.456$). Mean ALT and AST levels, mean $CD4^+$ T cell counts and HBe Ag prevalence were comparable between anti HDV positive and negative study participants with HIV/HBV co-infection.*

Conclusion: *Substantial number of HIV/HBV co-infected study participants were observed to be infected with HDV infection. We recommend the screening of HDV infection among HIV/HBV co-infected individuals to ensure their proper management.*

Keywords: *HIV infection, HBV co-infection, HDV infection.*

Introduction

In Africa, the prevalence of both HIV and HBV infection is high (O'Shea, 2010; UNAIDS, 2016). In Nigeria, the prevalence of HIV infection and HBV infection is 3.4 % and 13.6 % respectively (UNAIDS, 2015; Musa *et al*, 2015). The morbidity and mortality of liver diseases due to HBV infection increase in the setting of HIV/HBV co-infection, as a result of negative effect of HIV infection on the natural course of HBV infection (Thio, 2009).

Tropical and sub-Tropical regions have the highest prevalence of HDV infection and about 5 % of HBV infected patients may be affected by HDV infection (Sultanik and Pol, 2016). Hepatitis D Virus (HDV) infection occurs simultaneously with HBV infection or as super-infection of HBV infection (Greenwood, 1997; Sultanik and Pol, 2016). Both HBV and HDV infections may persist following HDV super-infection and the severity of HBV infection increases with HDV co-infection (Greenwood, 1997).

Fulminant hepatitis is more common in HDV/HBV co-infection than in HBV infection alone, HBV vaccine prevents HDV infection and HDV prognosis in the setting of HIV infection is open to doubt (Sultanik and Pol, 2016). Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) are some of the tests that measure liver cell integrity. Autoimmune manifestations, hepatocellular carcinoma and liver failure may follow as the complications of HDV infection (http: //www.emedicine.medscape.com/article/178038-overview).

DOI: 10.21522/TIJPH.2013.07.01.Art001
ISSN: 2520-3134

New drugs such as prenylation and myrcludex are active against HBV and HDV and are therefore promising for the treatment of HBV/HDV co-infection (Sultanik and Pol, 2016).

The screening of HDV infection is not a common practice in many health institutions and studies on HDV infection is limited in resource limited countries. Therefore, this study aimed at determination of HDV infection among HIV and HBV co-infected patients.

Methods

A cross sectional study was adopted in which 180 treatment-naïve HIV study participants were recruited into the study between March 2014 and October 2015. The study participants attended HIV clinic at Usmanu Danfodiyo University Teaching Hospital (UDUTH) Sokoto and Specialist Hospital Sokoto and approval for the study was obtained from the ethical committee of UDUTH Sokoto and Ministry of health Sokoto. Patients that were vaccinated for HBV infection were excluded from the study.

Data about the study subjects were obtained by employing interviewer administered technique using a questionnaire. Blood samples were obtained from the study participants after getting their informed consent and were screened for HBs Ag with HBs Ag ELISA kit (Fortress Diagnostic UK). Patients that were positive for HBs Ag were further screened for anti HDV with HDV IgG ELISA Kit (Perfemed South San Francisco the United States).

Patients who tested positive to anti HDV were further screened for HBe Ag using HBe Ag ELISA kit (DRG International Inc, USA), assessed for CD4+ T lymphocyte counts (Cyflow counter analyzer, PARTEC, Germany) and AST as well as ALT levels using Agappe Kit (Agappe Diagnostics, Switzerland; normal ranges of up to 46 IU/L and 49 IU/L respectively). These values were compared among variables of interest.

Statistical Package for Social Sciences (SPSS Version 20) was used for the data analysis. Student's t-test and Chi-square test were applied for the test of significance. Level of significance was set at $p \leq 0.05$.

Results

Of the 37 HIV infected study participants that were positive for HBs Ag, 4(10.8 %) were positive for anti HDV and therefore infected with HDV infection. Their age was 32 ± 10 (Mean ± SD) and comprises of 21(56.8 %) and 16(43.2 %) males and females respectively. (Table 1)

Table 1. Demographic data and prevalence of anti HDV among HIV/HBV co-infected study participants

Variable	HIV/HBV co-infection (n=37)
Anti HDV n (%)	4(10.8 %)
Age (years) Mean ± SD	32 ± 10
Sex	
Male n (%0)	21(56.8 %)
Female n (%)	16(43.2)

Influence of sex, age group, multiple sexual partners, blood transfusion and needle sharing in the acquisition of HDV infection.

There was no statistically significant age group and sex difference in the prevalence of HDV infection among the HIV/HBV co-infected study participants, though numerically higher among Females, 2(12.5 %) against 2(9.5 %) in Males ($P \leq 0.587$) and higher among age group 41-50, 1(14.3 %) compared to other age groups ($P \leq 0.671$). Subjects with history of multiple sexual partners (MSP), blood transfusion and needle sharing had higher percentage of HDV infection compared to subjects with negative history of

such variables even though there was no statistical significance (13.8 % Vs 0.0 %, P≤ 0.557), (33.3 % Vs 8.8 %, p ≤ 0.298), (20.0 % Vs 9.4 %, P≤ 0.456) respectively. Table 2 showed these results.

Table 2. Comparison of HDV infection in HIV/HBV co-infected study participants by sex and age group, and in study participants with and without multiple sexual partners, blood transfusion and needle sharing

Variable	HDV infection among HBV/HIV infected study participants n(%)	P-value
Sex		
Females (n=16)	2(12.5 %)	0.587
Males (n=21)	2(9.5 %)	
Age group	0(0.0 %)	0.671
≤ 20 (n=5)	2(12.5%)	
21-30 (n=16)	1(12.5 %)	
3-40 (n=8)	1(14.3 %)	
41-50 (n=7)	0(0.0 %)	
51-60 (n=1)		
Multiple sexual partners	4(13.8 %)	0.577
Yes (n=29)	0(0.0 %)	
No (n=8)		
Blood transfusion		
Yes (n=3)	1(33.3 %)	0.298
No (n=34)	3(8.8 %)	
Needle sharing		
Yes (n=5)	1(20.0 %)	0.456
No (n=32)	3(9.4 %)	

ALT and AST levels, CD4+ T cell counts and HBe Ag prevalence among study participants with and without HDV infection.

Mean ALT and AST levels were higher and lower respectively among HIV/HBV co-infected participants with and without HDV infection (P< 0.940; 0.390 respectively). The mean $CD4^+$ T cells count was lower among HIV/HBV co-infected participants with HDV infection though not statistically significant (P< 0.965). All the HBe Ag positivity occurred among HIV/HBV co-infected participants that were not positive for anti HDV 7(21.2 %), however, it was not statistically significant (P< 0.570). These results were shown in Table 3.

Table 3. Comparison of ALT and AST levels, CD4+ T cell counts and prevalence of HBe Ag among HIV/HBV co-infected study participants with and without HDV infect ion

Variable	HDV infection among HIV/HBV co-infected study participants (Yes=4) (No=33)	P-value
ALT levels (Mean ± SD)	32.2 ± 22.9 36.0 ± 27.4	0.940
AST levels (Mean ± SD)	32.0 ± 28.4 49.3 ± 38.4	0.390
$CD4^+$ T cell counts (Mean ± SD)	200 ± 146 205 ± 207	0.965
HBe Ag	0(0.0 %) 7(21.2 %)	0.570

DOI: 10.21522/TIJPH.2013.07.01.Art001
ISSN: 2520-3134

Discussion

The current study recorded lower sero-prevalence of HDV infection (10.8 %) among HIV/HBV co-infected study participants compared to a number of studies (Honge *et al*, 2014; Motamedifar *et al*, 2015; Coffie *et al*, 2017). However, the value recorded in the current study was higher compared to other values recorded in some studies across the world including Nigeria (Mendes-Correa *et al*, 2011; Katwesigye *et al*, 2016; Ifeorah *et al*, 2017). Lower value of triple infection of HIV/HBV/HDV obtained in same Northern part of Nigeria is in line with the view of some researchers that global HDV epidemiology is changing (Mumtaz *et al*, 2005).

The distribution of Delta virus infection was higher among female study participants than in males as well as among study participants that were 41-50 years compared to other age groups, though none was statistically significant. Similarly some studies did not observe association between HDV infection with age and or sex (Motamedifar *et al*, 2015; Coffie et al, 2017; Ifeorah *et al*, 2017). On the contrary, Mumtaz *et al*, (2005) in their study among HBV infected subjects, observed male gender and younger age to be associated with HDV infection.

The higher prevalence of HDV infection in HIV/HBV co-infected study participants with positive history of multiple sexual partners, needle sharing and blood transfusion even though not statistically significanct, is not unexpected because HBV and HDV infections have common routes (such as sexual and parenteral) of transmission (Greenwood *et al*, 1997; Sultanik and Pol, 2016). In contrast, Motamedifar *et al*, (2015) in their study recorded significant difference with regards to blood transfusion, however did not observe significant difference with regards to intravenous drug usage and unsafe sexual contact. Smaller sample size that were positive for HDV infection may be the reason for not observing statistical difference.

Study participants with tipple infection of HIV/HBV/HDV were observed to have higher mean ALT levels compared to those with HIV/HBV co-infection, though not statistically significant. Similarly, Motamedifar *et al*, (2015) and Katwesigye *et al*, (2016) in their studies did not record statistical difference with regards to ALT levels among HIV/HBV co-infected study participants with positive and negative anti HDV. Smaller number of study participants that were positive for anti HDV may probably have contributed to the lack of association. Higher mean ALT levels among Delta virus infected participants compared to non-Delta virus infected participants even though not statistically significant may be a pointer of adverse effect of HDV infection on liver cells and this may result in abnormal ALT levels. On the other hand, mean AST levels was higher among non-HDV infected than in HDV infected HIV/HBV study participants, however it was not statistically significant and this finding is comparable to what Motamedifar *et al*, (2015) and Katwesigye *et al*, (2016) documented in similarly related studies. The explanation of this finding in the current study is that, non-Delta virus infected study participants may probably have one or more of other disease conditions such as: myocardial infarction, acute haemolytic anaemia, skeletal muscle disorders and pancreatitis that may also cause AST elevation.

In the current study, HDV infection was observed not have effect on $CD4^+$ T lymphocytes count, though non-HDV reactive among HIV/HBV co-infected study participants had higher mean $CD4^+$ T lymphocytes count. This finding is comparable to what Katwesigye *et al*, (2016) obtained in their study.

Hepatitis B e antigen is a marker of HBV replication, is implicated in chronic course of HBV infection and its presence makes patient to be highly infectious. However, in the current study, HDV infection was observed not to have effect on HBe Ag expression, as all the HBe Ag positivity occurred among HIV/HBV co-infected study participants that were not positive for anti HDV even though not statistically significant. This may suggest that HDV infection in our study participants may be as a result of super infection and not a co-infection, as ‘’HDV super-infection may lead to HBe Ag sero-conversion.’’ (Sultanik and Pol, 2016).

Conclusion

Substantial HDV infection among HIV/HBV co-infected study participants was observed in the current study. In view of the need for additional medication required for the treatment of HDV infection, we therefore recommend HDV infection screening for HIV/HBV infected individuals. Inability to carry out HDV RNA which is the most important marker in the diagnosis and follow up of HDV infection was a limitation of the current study. Another limitation of this study was inability to screen for other disease conditions that may raise AST levels.

References

[1].Coffie PA, Tchounga BK, Bado G, Kabran M, Minta DK, Wandeler G et al. Prevalence of hepatitis B and delta according to HIV-type: a multi-country cross-sectional survey in West Africa. BMC Infectious Diseases 2017, **17**:466. https://doi.org/10.1186/s12879-017-2568-5.

[2].Greenwood D, Slack R and Peutherer J. *Medical Microbiology*: *A guide to Microbial Infections: Pathogenesis, Immunity, Laboratory Diagnosis and control 15th Edition*, Churchill Livingstone, Edinburg, England, 1997, pp 443, 446-447.

[3].Hønge BL, Jespersen S, Medina C, Té DdS, da Silva ZJ, Lewin S et al. Hepatitis B and Delta Virus Are Prevalent but Often Subclinical Co-Infections among HIV Infected Patients in Guinea-Bissau, West Africa: A Cross-Sectional Study. PLoS ONE 2014, 9(6): e99971. https://doi.org/10.1371/journal.pone.0099971.

[4].Ifeorah I, Bakarey AS, Adeniji A and Onyemelukwe N. Seroprevalence of Hepatitis B and Delta viruses among HIV infected population attending Antiretroviral clinic in selected health facilities in Abuja Nigeria. Journal of Immunoassay and Immunochemistry 2017, 10.1080/15321819.2017.

[5].Joint United Nation Programme on HIV/AIDS. Global AIDS Update. 2016 [Cited 2016, March 13]. Available at: http://www.unaids.org/site/default/media_asset/global-AIDSupdate-2016_en.pdf.

[6].Joint United Nation Programme on HIV/AIDS. Nigeria Global Acquired Immunodeficiency Syndrome Response Country Progress Report. 2015 [Cited 2017, March12]. Available at: *http://www.unaids.org/sites/default/files/countryNGA_narrative_report_2015.pdf*.

[7].Katwesigye E, Seremba E, Semitala F and Ocama P. Low Sero-prevalence of hepatitis delta antibodies in HIV/ hepatitis B co-infected patients attending an urban HIV clinic in Uganda. Afri Health Sci 2016, 16(4): 1089-1093. http://dx.doi.org/10.4314/ahs.v16i4.26.

[8].Mendes-Correa MC, Gomes-Gouvêa MS, Alvarado-Mora MV, Da Silva MH, Lázari C, Cavalcanti NCS, et al. Hepatitis delta in HIV/HBV co-infected patients in Brazil: is it important? International Journal of Infectious Diseases 2011, 15(12): pp e828-e832.

[9].Motamedifar M, Taheri M, Lankarani KB, Gholami M, Lari MA, Faramarzi H, et al. The Prevalence and Risk Factors of Hepatitis Delta Virus in HIV/HBV Co-Infected Patients in Shiraz, Iran, 2012. Iran J Med Sci 2015, 40(5): 448–453.

[10]. Mumtaz K, Hamid SS, Adil S, Afaq A, Islam M, Abid S et al. Epidemiology and clinical pattern of hepatitis delta virus infection in Pakistan. J Gastroenterol Hepatol. 2005, 20(10):1503-7.

[11]. Musa BM, Bussell S, Borodo MM, Samaila AA and Femi OL. Prevalence of hepatitis B virus in Nigeria, 2000-2013; A systemic review and meta-analysis. *Nigeria Journal of Clinical Practice* 2015, 18(2): 163-172.

[12]. O'Shea RS. Liver disease related to hepatitis B remains an important public health concern and major cause of morbidity and mortality. It also presents a common challenging problem for practicing physicians. 2010. [Cited 2012, December 10]. Available at: *www.clevelandclinicmeded.com/medicalpubs,hepatology/hepatitis-B.*

[13]. Roy PK. Hepatitis D: Background, Etiology, Epidemiology. [Cited 2018, January 10]. Availlable at: http://www.emedicine.medscape.com/article/178038-overview).

[14]. Sultanik P and Pol S. Hepatitis Delta Virus: E pidemiology, Natural Course and Treatment. J Infect Dis Ther 2016, 4:271. doi: 10.4172/2332-0877.1000271.

[15]. Thio CL. Hepatitis B and Human immunodeficiency virus infection. Hepatology 2009, 49(5); 138-145.