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Epstein - Barr Virus Capsid Antigen (EBV-VCA) IgM antibodies among HIV infected individuals in Jos, Nigeria.

Joseph Anejo-Okopi[1,2,*], Ocheme Julius Okojokwu[1], Nenkimwa Adamu[1], Juliet Ogbonna[1], Joshua Adetunji[1,3], Gabriel Odugbo Ikwulono[4]

[1]Department of Microbiology, Faculty of Natural Sciences, University of Jos, Nigeria
[2]AIDS Prevention Initiative in Nigeria, Jos University Teaching Hospital, Jos, Nigeria
[3]Medicom Laboratories Microbiology, Jos Plateau state, Jos, Nigeria
[4]National AIDS and STIs Control Program (NASCP), Federal Ministry of Health, Abuja, Nigeria
*Corresponding author: Joseph Anejo-Okopi (josephokopi@yahoo.com)

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Abstract Human immunodeficiency virus (HIV) infection is associated with an increased risk for Viral infections such as Epstein-Barr virus (EBV)infections also known as Human Herpes Virus Type 4 (HHV-4) and their related diseases which frequently cause malignancy related diseases resulting to poor treatment and health outcomes. In this study, we determined the seroprevalence of EBV VCA IgM antibodies among HIV patients attending Plateau Specialist Hospital, Jos, Nigeria and to evaluate their association with age, sex as well as other demographic factors. A total of 92 HIV positive patients were enrolled and serum samples were screened for antibodies using the ELISA kit. The prevalence of EBV VCA IgM was 6/92(6.53%), and mean age of 37.48 ±1.01 years. This study has contributed to baseline data, and suggest the need for larger studies and importance of screening and treatment of EBV among HIV patients.

Keywords: *Epstein-Barr Virus, VCA-IgM, HHV4, HIV, Seroprevalence, Nigeria*

1. Background

Epstein-Barr virus (EBV) also known as Human Herpes virus type-4 (HHV-4) belongs to the family of herpesviridae, Subfamily Gammaherpesvirinae, Genus Lymphocryptovirus and serves as the dominant cause of acute infectious mononucleosis in young children and adolescents [1], with about 90% of adults in the world have antibodies against EBV [2]. Primary acute EBV infections are largely asymptomatic and the latent infection could persist for the lifetime [3].

In few circumstances, chronic active EBV infections might lead to complications and death in immunosuppressed individuals [4]. EBV infections have been linked to hemophagocytic syndrome, a severe inflammatory illness, characterized by prolonged fever, cytopenia, and liver dysfunction [5,6]. Additionally, the virus is causally linked to several other malignancies, such as Burkitt's lymphoma, Hodgkin lymphoma, tumors in HIV-infected patients, and nasopharyngeal carcinomas [7-9]. Previous studies have estimated the sero-epidemiology in Europe and United States to be over 50% of adolescents would have been seropositive to EBV [10,3,11]. However, studies in Africa (Ethiopia and Nigeria) and Asia (Taiwan) have reported seroprevalence from 6%, 11% -17% [12-15], but data on the sero-epidemiology of EBV among HIV infected is still very scarce in Nigeria.

Several factors and analysis of risk factors such as; age, gender, country or region of residence, household educational level, kissing, smoking habit and sexual activity have been associated with the EBV seropositivity [16,17]. The use of

vaccination which is unavailable along with other public health measures can greatly reduce the co-morbidity burden of EBV infection among immunosuppressed individuals. The sero-epidemiological data would provide useful information for public health interventions towards target populations and development of an idea candidate vaccine. It is well known that EBV is a common opportunistic infection agent in the human immunodeficiency virus-infected individuals who are immunocompromised. In this study we conducted a small-scale study to describe the prevalence of specific antibodies (IgM) to EBV-VCA and demographic factors in Jos Nigeria.

2. Materials and Methods

2.1. Study Population

The HIV positive individuals attending plateau state specialist hospital Jos, Plateau State**,** Nigeria who consented were enrolled from October to December 2017. The patients bio data including clinical (CD4) and other relevant information were obtained using structured questionnaire and were assured of strict confidentiality of responses as specified in the ethical clearance guideline given for this study. Afterwards, blood sample was collected from each of the 92 enrolled patients. The study protocol was approved by Ethics Committee of Plateau State Specialist Hospital Jos, Plateau State according to the amended 1964 Helsinki Declaration.

2.2. Sample Collection

Blood samples were collected in tube with anticoagulant for serology. A tourniquet was firmly tied to the upper arm of the subjects while sitting and the skin was sterilized with 70% alcohol. The vacutainer needle was inserted into conspicuous antecubital vein and the plunger of the sterile syringe was withdrawn and pressure applied to the puncture site and apply dry cotton wool to stop bleeding and tubes were labelled appropriately. Blood samples were spun on a bench centrifuge at 3,000 rpm for 10 minutes to obtain sera. Aliquots of serum were made per sample in labelled sterile cryovials which were stored at −20°C until ready for analysis.

2.3. Qualitative testing of anti- EBV IgM antibodies

The commercial enzyme-linked immunoassay (ELISA) kit Golden Bio Technologies Corp, CA 91786, U.S.A was used to detect anti-EBV viral capsid antigen (VCA) IgM in sera. The assay was performed in accordance with manufacturer's instruction. Briefly, the diluted patient serum was added to wells coated with purified antigen, and the plate was incubated with 100µl of diluted serum at room temperature for 30 minutes. After washing for three times, peroxidase-conjugated anti-human IgM was added and incubated at room temperature for 30 minutes. After another washing for three times, the plate was incubated at room temperature for 15 minutes to allow the hydrolysis of the substrate by the Enzyme. The kit provided ready-to-use positive controls negative controls and calibrators ((IgM, human). Excess enzyme conjugate is washed off and substrate is added. The reaction was stopped and the optical density was measured at 450nm. The intensity of the color generated is proportional to the amount of IgM specific antibody in the sample. The standard curve was established by calibrators and used to calculate virus-specific antibody concentration, and the result was interpreted according to the manufacturer's instruction.

2.4. Statistical Analysis

The data obtained from the study were subjected to descriptive statistical analysis. Statistical analysis of results was done using SPSS 20.0 statistical software. Chi square was used and $P<0.05$ was considered to be significant. Adjusted odd ratio was used to determine the association between the infection and the risk factors. SPSS program for Windows (V.21.0; SPSS, Inc., Chicago, IL) was used.

3. Result

Total of 92 patients were enrolled, 6 were positive for EBV-VCA IgM antibodies, therefore the prevalence of EBV infection among HIV infected patients in Jos Metropolis was 6.53% as summarized in Table 1 showing the mean age of patients was 37.48 ±1.01 years. The table also showed summary of the distribution of EBV infection among age groups, sex, marital, employment, educational, duration of ART and CD4 status of the individuals. High prevalence (7.50%) was observed among the age group of 31-40 years with no significance difference (p=0.13). in the sex category, the prevalence among the female was 8.51%, male (4.45%) p=0.76, while the marital status, the prevalence was high among the widowed (7.70%), single/separated (5.46%), married (5.89%), with no significance difference (p=0.42). For the employment status, the prevalence was high among the unemployed group (8.16%), employed (4.65%), p=0.82, while the prevalence among the duration on ART; 0-1 years (11.43%, 2-4 years (6.67%), ≥5 years (2.38%), p= 0.68. For the educational status; the prevalence was high among those with secondary school (8.00%), Primary (6.38%), tertiary (5.00%), p=0.68. Based on the CD4, the patients were into two; <500, and ≥500, the prevalence was higher among the former category (7.94%), with no significance difference (p=0.062). There was no statistical difference in the seroprevalence of EBV-VCA IgM antibodies between the subgroups.

Table 1. Prevalence of EBV IgM infection in relation to Age, Sex, marital, employment, duration of ART, Educational and CD4 Status among HIV infected patients.

Characteristic	No Patients	NO. Positive (%)	P- value
Age			0.13
18-30	18(19.56)	1(5.55)	
31-40	44(43.48)	3(7.50)	
41-50	25(27.17)	1(4.00)	
≥ 51	19(20.65)	1(5.26)	
Sex			0.76
Male	45(48.91)	2(4.45)	
Female	47(51.09)	4(8.51)	
Marital status			0.42
Married	34(36.96)	2(5.89)	
Single/Separated	55(59.78)	3(5.46)	
Widowed	13(14.13)	1(7.70)	
Employment status			0.82
Employed	43(46.74)	2(4.65)	
Unemployed	49(53.26)	4(8.16)	
Duration on ART			0.68
0-1 Years	35(38.05)	4 (11.43)	
2-4 Years	15(16.31)	1(6.67)	
≥ 5 Years	42(38.29)	1(2.38)	
Educational Status			1.09
Primary	47(51.09)	3(6.39)	
Secondary	25(27.18)	2(80.00)	
Tertiary	20(21.74)	1	
CD4 Count.			0.06
<500	63(68.48)	5(7.94)	
≥500	29(31.53)	1(3.45)	

4. Discussion

Epstein Barr virus is one of the leading cause of comorbidity and malignancies such as Burkitt ś lymphoma and nasopharyngeal carcinoma in HIV-positive individuals due to immunosuppression. EBV has been identified as a major contributing factor to the pathogenesis of most of lymphoproliferative diseases, including Orapharyngeal and leukoplakia in HIV positive patients [5]. The presence of anti-VCA IgM antibodies shows acute primary EBV infection which are usually produced transiently in the early course of illness and disappear within 4 to 6 weeks [18]. The appearance of EBV VCA IgM in HIV positive individuals indicate the presence of the virus and suggestive of acute infection [19]. Though the symptomatic status of EBV infection was not established in the study population, but it was unclear about the level of subclinical EBV infections and its role in the transmission of virus in the Nigerian population. To better understand the interaction among the age of EBV acquisition, the development of either symptomatic or subclinical illness, and the risk of EBV-associated malignancies, further longitudinal studies is suggested to address the epidemiology in the HIV population and the immune correlate of protection against virus.

The observed prevalence (6. 53%) was high compared to earlier study done in south west Nigeria which recorded 4% [13], but similar to another finding in Zaria, Northern Nigeria with prevalence of 6.6% [12]. The highest prevalence of anti-EBV IgM (5.81%) was in the age range (31-40) years. This may be due high sexual activities and networking amongst other factors such as assayed antibody type, geographical location as well as low living standard of the study population as compared to the age range mentioned in earlier reports, and its corroborates with earlier reported studies [20,21] that age range 21-40 and 30 ≤ 40 have the highest EBV antibody incidence, respectively. The prevalence was higher among the females, however, with no significance and this was agreement with other reported studies [22,23]. Although underlined mechanisms involving high EBV antibodies in females remain unclear, but the reason could be frequent contacts with children than men.

The sero-epidemiological pattern of EBV infection which is obvious with other infectious diseases could be affected by different factors such as; the public health policy, sexual practice, hygiene behavior, and socio-economic status. In the study, we observed high prevalence among the widows, unemployed secondary level of education and those who are on ART less than 1 year, but with no statistical significance, although the definition of these factors could vary in different population and countries. We observed that CD4 cell count was associated with the EBV seropositive rate in Nigeria, this corroborated with recent study done by Abdollahi et al. (2014), which suggested that low CD4+ cell count may be an

indication of poor clinical outcomes. This in effect, may have higher chances of associated malignancies and or other opportunistic infections. Though the low $CD4^+$ cell count (<500 cells/mm^3) observed had no significant association, and this was corroborated with earlier reported studies [12,21]. This may also be due to transmission pattern proposed of adults acquiring higher viral dose through sexual activity than children do through salivary contact [17,24]. Taken together, low $CD4^+$ cell count may suggest poor outcome of HIV infection as mentioned earlier [21].

This study bears some limitation such as the study design and small sample size which may not permit generalization of our findings. Future larger and multicenter clinical research are suggested to address some unanswered sero-epidemiological questions.

Conclusion

The current study showed high of EBV anti-EBV IgM in HIV-positive patients, and with the causal link of EBV and certain lymphoma associated malignancies in HIV positive adults. This data suggest that there may be cases of infectious mononucleosis among populations at risk such as HIV infected and that clinicians and other healthcare should look out for it. In view of this screening strategies and awareness by non-profit organizations and healthcare workers should be put in place for early detection and prompt antiviral treatment. Also awareness on hygiene practices as preventive methods to reduce infection rates in the general and risk population. The development of effective and use of EBV vaccine could substantially reduce the disease burden due to primary EBV infection and incidence of infectious mononucleosis and associated human malignancies such as Hodgkin's disease, endemic Burkitt's lymphoma, and nasopharyngeal carcinoma. Further larger study is needed to investigate both prevalence and incidence among the general and target populations.

Conflict of interest

The authors declared that there is no conflict of interests regarding the publication of this article.

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References

[1] Balfour HHJr, Sifakis F, Sliman JA, Knight JA, Schmeling DO, Thomas W. Age-specific prevalence of Epstein-Barr virus infection among individuals aged 6–19 years in the United States and factors affecting its acquisition. J Infect Dis, 2013; 208: 1286–1293

[2] Rickinson AB, Kieff E. Epstein-Barr virus. In: Virology (eds. DM Knipe, PM Howly) 5th ed., Vol. 2, Wolters Kluwer /Lippincott Williams & Wilkins, Philadelphia, 2006; pp. 2655-2700.

[3] Cohen JI. Epstein-Barr virus infection. N Engl J Med, 2000; 343: 481–492.

[4] Tsai MH, Hsu CY, Yen MH, Huang YC, Lin SJ, Lin TY et al. Epstein-Barr virus-associated infectious mononucleosis and risk factor analysis for complications in hospitalized children. J Microbiol Immunol Infect, 2005; 38: 255–261

[5] Kimura H, Hoshino Y, Kanegane H, Tsuge I, Okamura T, Kawa K, Morishima T. Clinical and virologic characteristics of chronic active Epstein-Barr virus infection. Blood, 2001; 98: 280–286

[6] Chen CJ, Huang YC, Jaing TH, Yang CP., Chang LY, Lin TY et al. Hemophagocytic syndrome: a review of 18 pediatric cases. J Microbiol Immunol Infect, 2004; 37: 157–163

[7] Carbone A, Cesarman E, Spina M, Gloghini A, Schulz TF. HIV-associated lymphomas and gamma-herpesviruses. Virus Research, 2009; 143, 209-221.

[8] Thorley-Lawson, D.A., Gross, A. Persistence of the Epstein-Barr virus and the origins of associated lymphomas. N Engl J Med, 2004; 350: 1328–1337.

[9] Bertrand AK, Birmann MB, Chang ET, Spiegelman D, Aster J C, Laden F et al. A prospective study of Epstein-Barr virus antibodies and risk of non-Hodgkin lymphoma. Blood, 116 2010; 3547-3553

[10] Kangro HO, Osman HK, Lau YL, Heath RB, Yeung CY, Ng MH. Seroprevalence of antibodies to human herpesviruses in England and Hong Kong. J Med Virol, 1994; 43: 91–96.

[11] Dowd JB, Palermo T, Brite J, McDade TW, Aiello A. Seroprevalence of Epstein-Barr virus infection in U.S. children ages 6–19, 2003–2010. PLoS One, 2013; 8: e64921.

[12] Bishop GH, Adegoke OO. Seroprevalence of Epstein-Barr Virus IgM Antibodies among HIV-Patients and Apparently Healthy Blood Donors Attending Ahmadu Bello University Teaching Hospital, Shika-Zaria, Nigeria. International Journal of Scientific Research in Knowledge, 2016; 4(5): 105-111

[13] Kolawole OE, Kola OJ, Elukunbi AH. Detection of Epstein-Barr virus IgM in HIV infected individuals in Ogbomoso, Nigeria. British Journal of Virology, 2017; 3(6): 177-182.

[14] Ibrahim MH, Faten R, Abdel Ghaffar ARF, El Shaer ER, Madian AM. Prevalence of Epstein-Barr Virus and Hepatitis B Virus Infections among Chronic HCV PatientsAttending Kafer El Shiekh Liver and Heart Institute, Egypt. Journal of Advances in Medicine and Medical Research (JAMMR), 2018; 26(8): 1-8,

[15] Chen CY, Huang KYA, Shen J-H, Tsao K-C, Huang Y-C. A Large-Scale Seroprevalence of Epstein-Barr Virus in Taiwan. PLoS ONE, 2015; 10(1): e0115836.

[16] Higgins CD, Swerdlow AJ, Macsween KF, Harrison N, Williams H, Crawford A et al. Study of risk factors for acquisition of Epstein-Barr virus and its subtypes. J Infect Dis. 2007; 195(4):474-82.

[17] Crawford DH, Swerdlow AJ, Higgins C, McAulay K, Harrison N, Williams H et al. Sexual history and Epstein-Barr virus infection. Infect. Dis. 2002; 186:731–736.

[18] Jenson, H. B. Epstein-Barr virus. Pediatr Rev, 2011; 32: 375–383.

[19] Arotiba JT, Adebola AR, Iliyasu Z, Babashan M, Ladipo MMA, Osude OD et al. Oral manifestations of HIV/AIDS infection in Nigerian patients. Nigerian Journal of Surgical Research, 2005; 7, 176-181

[20] Chakraborty N, Bhattacharyya S, de Mukherjee CA, Bhattacharya D, Santra S, Chakrabarti. S et al. Incidence of multiple herpesvirus Infection in HIV seropositive patients, a big concern for Eastern Indian scenario. Virology Journal, 2010; 7, 147: 1-7

[21] Abdollahi A, Shoar S, Rasoulinejad M, Sheikhbahaei. S Sero-prevalence of Epstein - Barr virus among HIV positive patients moreover and its association with CD4 positive lymphocyte count. Acta Medica Iranica, 2014; 52(12), 916-921

[22] Adjei AA, Armah HB, Gbagbo F, Boamah I, Adu-Gyamfi C, Asare I. Seroprevalence of HHV-8, CMV, and EBV among the general population in Ghana, West Africa. BMC Infect Dis, 2008; 8: 111.

[23] Wagner HJ, Hornef M, Teichert HM, Kirchner H. Sex difference in the serostatus of adults to the Epstein-Barr virus. Immunobiology, 1994; 190: 424-429

[24] Balfour HHJr, Odumade OA, Schmeling DO, Knight JA, Vezina HE, Hogquist KA et al. Behavioral, virologic, and immunologic factors associated with acquisition and severity of primary Epstein-Barr virus infection in university students. J Infect Dis, 2013; 207: 80–88.