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Seroprevalence of Epstein Barr Virus among HIV Positive Patients Attending Federal Medical Center, Katsina State-Nigeria

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ABSTRACT

Background: Epstein-Barr virus (EBV) is a gamma herpes virus that infects 95% of the human population. Primary infection is often asymptomatic but results in lifelong infection, when immune is compromised EBV is associated with lymph proliferative diseases and malignancies such as Burkitt´s lymphoma, Nasopharyngeal Carcinoma, and Hodgkin's lymphoma. This study was designed to determine the prevalence of EBV in Human immune-deficient virus (HIV)-infected individuals in Katsina State, Nigeria. **Materials and Methods:** Two hundred and seventy- three (273) consented HIV-infected individuals were screened for EBV antigens, for the period of five months (November 2018- March 2019). The sera of individuals were subjected to antigen serological assay by enzyme-linked immunosorbent assay. **Results:** Out of 273 subjects that were tested 89(32.6%) were EBV antigen positive and 184(67.4%) were EBV antigen negative, prevalence of EBV antigen was higher in females with 61(22.3%), age group 35-44 years 30(10%), CD4+ 425-524 cells/µl 20(7.4%), and viral load 48(18.6%) with less than 1000 count. **Conclusion**: This study has contributed baseline data and provided insights in EBV-HIV co-infection in Katsina Northwestern Nigeria This would undoubtedly serve as a basis for further studies on EBV in the general population.

Key words: Enzyme-Linked Immunosorbent Assay, Epstein-Barr Virus Infections, HIV , Prevalence, Nigeria.

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INTRODUCTION

Epstein Barr virus (EBV) was named after Michael Anthony Epstein and Yvonne Barr who discovered and documented the virus (1) Epstein Barr virus (EBV) is also called human herpes virus 4 (HHV4). It is a virus belonging to family *Herpesviridae*, subfamily Gamma *Herpesvirinea* and genus Lymphocriptovirus (2). EBV has icosahederals symmetry that compose of 172kb, 162 capsomeres, enveloped, double stranded DNA genome encapsulated by nucleocapsid tegument protein and membrane carrying various surface glycoprotein's, mature virions are approximately 120 to 180 nm in diameter (2). Two strains, or types, of EBV infect humans (3). These strains differ in the sequences of the viral genes expressed during latent infection and in their ability to transform B lymphocytes[3]Although earlier studies suggested that type A (or EBV-1) virus infection was more prevalent in North America and Europe and that type B (or EBV-2) virus infection was more prevalent in Africa, more recent studies suggest that both strains are prevalent in the United States (4) and that persons can be coinfected with both strains. Like other gamma herpes viruses, EBV establishes latent infection in lymphocytes and can induce proliferation of the latently infected cells (5).

EBV attaches to B cells via binding of the viral gp350 protein to CD21 on B cells (5) EBV gp42 then interacts with B-cell Human Leucocyte Antigen (HLA) class II molecules and triggers fusion with the host membrane in epithelial cells (3, 5).

In a recent cross-sectional survey conducted to determine the seroprevalence of various viral among HIV-infected individuals, EBV prevalence of 96.6% was observed in China, also found a very high seropositivity of 98% and 92.5% in HIV positive and HIV negative males, respectively (6). No well-defined studies from northwestern part of Nigeria have been carried out in HIV-infected individual to assess the co-morbidities associated with EBV.

EBV Viral coinfections in HIV positive patients and acquired immunodeficiency syndrome (AIDS) are major health concerns all over the world. As a result of the interaction between HIV status and other viral infections, changes in severity or the progress of both infections may occur. However, opportunistic infections are the leading cause of hospitalization and morbidity among HIV-positive patients leading to significant mortality in this population. The role of the EBV in clinical complications and disease progression among HIV-AIDS patient remain unclear, this particularly so in northern region of Nigeria.

The aims of this study is to determine the prevalence of EBV infection among HIV positive population in Katsina, Nigeria.

MATERIAL AND METHODS

Study Area

This study was conducted at Federal Medical Center Anti Retro Viral clinic. Katsina, the capital of the Katsina State, it has a geographical coordinates of latitude 12°58'53.62"N and a longitude of 7°37'20.16"E covers a total area of 24,192 square kilometers (9,341 sq mi), 519m elevation above sea level.

Ethical Clearance and informed consent

Ethical clearance was sought and obtained from the ethical and human research committee of Federal Medical Center Katsina (FMCNHREC.REG.N003/0802012).

Informed consent was obtained from all participating subjects in accordance with the standards of human experimentation and with the Helsinki Declaration of 1975, as revised in 2003. This was done via an informed

consent medical history, provisional diagnosis, clinical and other laboratory findings result was asked

Sample collection, preparation and separation

Ten milliliter of blood sample was collected from individual participants using standard venipuncture phlebotomy with serum separation tubes (7). The tubes was labeled appropriately with participant's identification number. Sera from these blood samples was separated by allowing the blood to clot at room temperature then by centrifugation at 2500rpm for 10 minutes. The serum was aspirated into the cryovial containers and stored at - 20^{O}C at hematology laboratory of Federal Medical Center Katsina, before laboratory analysis.

Serology, CD4 and viral load count. All the 273 samples were subjected to Epstein-Barr virus specific Enzyme Linked Immunosorbent Assay (ELISA) using the Epstein-Barr virus antigen detection ELISA kit (Melsin Medical Co., Limited Changchun, China). CD4 was determine using (CyflowPartec counter version 2) and viral load count was determine using (Real time PCR).

Statistical analysis: Data obtained were subjected to descriptive analysis. Chi square was determined at 95% intervals using SPSS program for windows version 20.

Table1: Prevalence of Epstein Barr virus among study population in relation to gender

	Results		
Gender	Positive	Negative	Total
Male	28 (34%)	54 (65.8%)	82 (30%)
female	61 (31.9%)	130 (68%)	191 (70%)
Total	89 (32.6%)	184 (67%)	273

Table 1 shows the prevalence of EBV according to gender. x^2 (1) = 0. 028. *P* value =0.867

Table 2: Age range distribution of EBV infection among HIV Positive Patients

Age	**Positive**	**Negative**	**Total**	**Chi square p value**
≤15	9 (3.2%)	12 (4.1%)	21 (7.3%)	
15-24	5 (1.8%)	14 (5.2%)	19 (7.0%)	
25-34	27 (9.8%)	43 (13.9%)	70 (23.7%)	
35-44	30 (10.9%)	76 (27.9%)	106 (38.8%)	
45-54	9 (3.2%)	29 (10.6%)	39 (13.8%)	
≥55	9 (3.1%)	15 (5.5%)	21 (8.6%)	
Total	89 (32.6%)	184 (67.4%)	273 (100)	0.271

Table 2 shows the prevalence of EBV according to age range and number tested and positive among the HIV positive patients

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Table 3: Prevalence of Epstein Barr virus among HIV positive patients in respect of socio-demography

Demographics		Positive	Negative	Total	chi square p value
Educated	Primary	21 (7.7%)	25 (9.2%)	46 (16.8%)	
	Secondary	28 (10.3%)	52 (19.4%)	80 (29.3%)	
	Tertiary	12 (4.3%)	43 (15.8%)	54 (19.8%)	
Uneducated		28 (10.3%)	64 (10.3%)	92 (10.3%)	
Total		89 (32.6%)	184 (67.4%)	273 (100%)	0.045
Employment status					
	Employed	39 (14.3%)	87 (31.9%)	126 (46.2%)	
	Unemployed	50 (18.3%)	97 (35.5%)	147 (53.8%)	
Total		89 (32.6%)	184 (67.4%)	273 (100%)	0.001
Residential area					
	Rural	19 (7.0%)	22 (8.1%)	184 (67.4%)	
	Urban	69 (25.3%)	162 (60.2%)	89 (32.6%	
Total		89 (32.6%)	184 (67.4%)	273 (100%)	0.11

Table 4: Correlation of Epstein Barr Virus Status of HIV Positive patients with CD4+ Value range

Gender	≤ 500 Cells/ul of Blood		≥500 Cells/ul of Blood	
	Positive	**Negative**	**Positive**	**Negative**
Female	37 (13.6)	58 (21.3)	25 (9.2)	74 (27.1)
Male	19 (7.0)	16 (5.9)	8 (2.9)	36 (13.2)
Total	**56 (20.6)**	**74 (27.2)**	**33 (12.1)**	**110 (40.3)**

Table 4 shows the gender distribution of CD4+ Value range in relation to positivity and negativity to EBV among the study population. (x^2 = 0.17 *p*= 0.017 df= 1)

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DISCUSSIONS

EBV has ability to establish lifelong latency and intermittent reactivation after primary infection and with limited clinical symptoms in the majority of infections (8). EBV is one of the leading opportunistic infection among HIV positive cohorts and contributing factor to pathogenesis of lymph proliferative disease such as oral hairy leukoplakia, and malignancy association with HIV positive patients which varies from primary etiologic agent to necessary contributing cofactor of Burkitt´s lymphoma, Nasopharyngeal Carcinoma and Hodgkin lymphoma (9). The prevalence in the current study was 32.6% Similar studies was conducted in other parts of the world including china, Malawi, Kenya, and India with observed prevalence of 58.0%, 89% 73% and 82%, as respectively (10, 11, 12, 13). The variation of the prevalence might be due to the fact that their research was Nucleic acid detection, differences in geographical location and socioeconomic status that are reflected by crowdedness and hygiene (14).

Prevalence of EBV antigen by gender distribution, the highest prevalence of current studies was found among females with 22.3% in accordance with the findings reported elsewhere (12, 15, 16, 17). The findings is in contrast with findings of (9, 10, 18) where the incidence was dominant in the male population rather than the female. This difference is in the notion that females amount more in the study subjects than the male, it might also be as a result of high record of sexual activeness in females than their male counterpart in the study area which prone them to more exposure.

In respect of the age group the highest incidence of EBV antigen 10.9% was in the age range 30-44 years. The current findings of EBV antigen prevalence is in accordance with age group as also earlier studies conducted [18 9] that age range 21-40 and 30 ≤ 40. However, it is in contrast with this studies carried out (15, 16) the age range of (41-50) years have the highest EBV incidence, respectively. The difference can be attributed to difference in geographical location, sexual activity as well as living standard of the study subjects as compared to the age range mentioned in earlier reports.

The CD4+ cells count of HIV positive patients showed that 42 (15.5%) of the patients that are EBV antigen positive had less than 500cells/mm^3. Low CD4+ count was an indication of progressed AIDS, with higher chances of developing more malignancies such as Burkitt's lymphoma, nasopharyngeal carcinoma, and Hodgkin's lymphoma among others. The current studies is in agreement with earlier findings .EBV is most frequently isolated from HIV-patients because of their low immune status promotes reactivation/proliferation of the virus (16, 19).

Despite receiving HAART for at least six months this studies observed that 48(18.6%) of EBV antigen was detected among HIV-positive patient with less than 1000 copies of HIV viral load count; while 41(16.0%) have more than 1000 copies HIV viral load count, this indicate there is no significant association between EBV and HIV viral load count and coincide with earlier report (10, 20, 21).

Conclusion

This study revealed a high prevalence of EBV in HIV population Katsina Northwestern Nigeria.

This study has contributed baseline data and provided insights in EBV-HIV co-infection in Katsina Northwestern Nigeria.

Recommendations

- The development of effective and use of EBV vaccine could substantially reduce the disease burden due to primary EBV infection

- Health education on preventive measures is expedient in reducing the EBV infections rate.
- Further studies should be conducted to have more data on circulating EBV in northwest and Nigeria.

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