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PREVALENCE OF HIV SEROPOSITIVITY IN PATIENTS WITH LYMPHOID MALIGNANCIES IN A TERTIARY CENTRE IN SOUTHERN NIGERIA.

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ABSTRACT

Objective: The human immunodeficiency virus (HIV) epidemic has a significant impact worldwide and infected subjects are at increased risk of developing cancer. We aim to determine the HIV seropositivity of lymphoid malignant patients in a tertiary centre in Southern Nigeria.

Method: The course of disease in 275 patients with lymphoid malignant disorders at the University of Benin Teaching Hospital, Benin City, Nigeria, was analysed from 1996 to 2006. Blood specimens screened for antibody to HIV infection were confirmed by Western blot and the CD4+ lymphocyte count was measured by flow cytometry technique.

Results: A total of 275 patients aged 18-72years were studied. Of the 275 lymphoid malignancies 11 cases were found to be HIV seropositive giving a seroprevalence of 4%. The most frequent lymphoid malignancy in association with HIV seropositivity was non-hodgkin's lymphoma (NHL) with a prevalence of 4.12% over the less frequent lymphoid neoplasms. The overall median CD4+ lymphocyte count was 185µl with 9 cases seropositive for HIV below 200µl ($P<0.0001$).

Conclusion: We conclude that the seroprevalence of HIV infection in patients with lymphoid malignancies was 4% with NHL being the most common neoplasm associated with HIV infection in concordance with studies in the Diaspora.

Key Words: HIV seropositivity; lymphoid malignancies. *(Accepted 10 March 2008)*

INTRODUCTION

Human immunodeficiency virus (HIV) epidemic in African subcontinent has a significant impact in Nigeria and infected subjects are at increased risk of developing cancer, particularly in the later stages of Acquired immunodeficiency syndrome (AIDS).[1] Also, haematological malignancies are not uncommon in our area. Due to inadequate diagnostic facilities and lack of health education, they are diagnosed at an advanced stage when treatment is either impossible or very difficult. Following the outbreak of HIV infection in 1981 there has been a widespread increase in the incidence of HIV-associated malignancies including non-Hodgkin's lymphoma (NHL), kaposi sarcoma and squamous cell carcinoma of the cervix.[2] It has been suggested that HIV may indirectly encourage the development of malignancies by initiating the release of cytokines which stimulate B-cell proliferation.[3,4] The continuous stimulus to B-lymphocytes may permit mutations in critical oncogenes or tumour suppressor genes, eventually resulting in malignant transformation. Though several studies have been done on HIV infection in this environment, none of these studies has addressed the association of HIV infection with lymphoid malignancies. The dearth of information linking HIV infection with lymphoid malignancies in this area thus necessitated this study. The objective of this study is to document the incidence of HIV seropositivity in patients with lymphoid malignancies in a tertiary centre in Southern Nigeria.

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PATIENTS AND METHODS

The course of disease in 275 patients with lymphoid malignant disorders was analyzed in a referral center retrospectively (n=201;1996-2003) and prospectively (n=74;2004-2006). These were patients attending the Haemato-Oncology and HIV/AIDS pilot project, PEPFAR (President Emergency Plan For AIDS Relief) at University of Benin Teaching Hospital (UBTH), a major referral center serving the Niger Delta region of Nigeria. Clinicopathologic profile and demographic features were obtained in detail. Histological analysis of lymph node biopsies from the patients served to establish the diagnosis of the various lymphoid malignancies. Histopathologic classification was

done according to the modern system of International Working Formulation.[5] Recordings of peripheral blood film and bone marrow aspiration cytology and trephine biopsy were taken. Blood specimens were screened for antibody to HIV infection using ELISA technique and confirmed by Western Blot while the CD4+ lymphocyte count was measured by the Partec IVD Flow-Cytometry based technique.

RESULTS

A total of 275 patients with a diagnosis of lymphoid malignancy aged 18-72 years with a median age of 45 years over an 11-year period were reviewed. This comprised 170 (61.8%) NHL patients, 60(21.8%) chronic lymphocytic leukaemia (CLL) patients, 35(12.7%) Hodgkin's lymphoma (HL) patients and 10(3.6%) acute lymphoblastic leukaemia (ALL) patients based on confirmed histological examination of excised lymph nodes and bone marrow aspiration cytology. These were 92 males (33.5%) and 183 females (66.5%) with a male-to-female ratio of 1:2. The overall median age for NHL, HL, CLL and ALL was 39, 33, 56 and 24 years respectively.

Of the 275 lymphoid malignancies, 11 cases were found to be HIV seropositive. These include 7(2.55%) NHL, 2(0.73%) CLL and one each (0.36%) for HL and ALL patients respectively. These 11 cases consist of 5 males (45.5%) and 6 females (54.5%) with a mean age of 42±12.7 years (range, 20-59 years). Seven (4.12%) of 170 NHL cases, 2(3.33%) of 60 CLL cases and 1 each of the 35 (2.86%) HL and 10 (10%) ALL cases encountered were confirmed seropositive for HIV antibody (table 1). Baseline characteristics of study patients revealed that performance status (PS) as assessed according to the Eastern Cooperative Oncology Group (ECOG) scale had all the patients within the worst scale (2-4). Among the lymphoid malignancies with HIV seropositivity, NHL was the most frequent. Seropositivity was observed in 3 patients each with high and intermediate grade lymphoma and only one case with low grade lymphoma (table 2). The Binet Clinical staging system showed that the 2 CLL seropositive patients presented in advanced stages B and C. The haematological blood findings showed various degrees of cytopenias. The overall median CD4+ lymphocyte count was 185µl with 9cases seropositive for HIV below 200µl (P<0.0001). The median CD4+ lymphocyte count for high grade and intermediate grade lymphoma was 150µl and 192µl respectively (P=0.04). The median survival of the series is 4 months in comparison to 9 months for patients with lymphoid malignancies who were seronegative for HIV. As at the time of writing this report, only one of the NHL-HIV patients was alive as they presented in advanced stage of the disease. They died of complications arising from HIV infection (n=3) while the others (n=7) died of disease progression/complications related to their lymphoid disease.

Table 1: **The Prevalence, Age and Sex Distribution of Patients with Lymphoid Malignancies and HIV Seropositivity.**

Variables	Lymphoid Malignancies			
	NHL (n=170)	CLL (n=60)	HL (n=35)	ALL (n=10)
Prevalence (%)	61.8	21.8	12.7	3.6
Age (years)	39	56	33	24
HIV seropositivity (%)	4.12	3.33	2.86	10.0
HIV Sex ratio (M:F)	3:4	1:1	0:1	1:0
Performance status				
0-1	0	0	0	0
2-4	7	1	2	1

Table 2:**Histopathological Profile and CD4+ Lymphocyte Count of HIV Patients with Lymphoid Malignancies.**

Histologic Diagnosis	CD4+ Lymphocyte Count
1. Non-hodgkin's lymphoma subtypes	
Follicular, predominantly l	195
Diffuse, mixed small and large cell	180
Diffuse, large cleaved cell	200
Diffuse, large cleaved cell	190
Lymphoblastic	146
Large cell immunoblastic	185
Non-Burkitt's	150
2. Hodgkin's lymphoma	
Mixed cellularity	198
3. Chronic lymphocytic leukaemia	158
4. Chronic lymphocytic leukaemia	170
5. Acute lymphoblastic leukaemia (L2 type)	200

DISCUSSION

Viruses are aetiologically linked to approximately 20% of all malignancies worldwide and HIV accounts for a significant cancer burden.[6] Lymphoid malignancies have been reported to be on the increase since the outbreak of HIV infection.[7,8] It is still not clear why HIV infected subjects have a predisposition for mainly B-lineage derived malignancies; though multifactorial reasons have recently been suggested.[3,4,6] However, improved diagnostic techniques, effects of the HIV epidemic, immunosuppressive therapies have been reported to account for only one-third of this increase.[9,10] The most frequent lymphoid malignancy in association with HIV seropositivity was NHL with a prevalence of 4.12% over the less frequent lymphoid neoplasms. The predominance of the NHL tumour in this study was obvious. This is similar to the findings in Baltimore, USA[6,7] and Siriraj hospital, Thailand.[11] Although there has been a rising trend of AIDS associated NHL worldwide, in the developing countries, the risk appears to be much lower as observed in previous studies.[8,12] This may be

attributed to lack of investigative facilities and earlier death from AIDS manifestations. The HIV infected patients had predominantly high and intermediate grade (diffuse large cell) lymphoma, a finding consistent with other previous studies.[12,13] Unlike the NHL-HIV infection which was predominant in this study and other previous studies, there was a high incidence of non-AIDS defined cancers reported in HIV infected subjects in Germany when compared to the general population.[14] The paucity of follicular type of NHL in this study may be due to the late presentation of diseases, ignorance and poverty including other strong limiting factors. With the improving survival of AIDS patients however, there may well be an increase in new discovery of non-AIDS related malignancies.

The other less frequent lymphoid malignancies found associated with HIV infection were CLL (3.33%), HL (2.86%) and ALL (10%). The apparent high percentage for ALL may be due to the small number of diagnosed ALL patients within the study period. Over the past 2 decades it has been reported that the CLL-HIV infection has significantly increased.[15] This may be related to the different age ranges for CLL and HIV infections. Unlike NHL, HL-HIV infection rarely develops and its characteristics are not well defined. In a Cooperative Study Group of malignancies associated with HIV infection, it was reported that HL is not an AIDS-defining disease.[1,16,17] The only HL patient associated with HIV seropositivity in this study had mixed cellularity histology similar to previous studies with an atypical aggressive clinical course resulting in early death within few months of first presentation.[18,19] All the lymphoid neoplastic-HIV infected patient population presented within the worst PS scale (2-4) which is typical of our cancer patients in this environment.[20]

Despite the advent of HAART, malignancy is a leading cause of morbidity and mortality since HIV infection presents additional challenges to management. Majority of the patients were treated with systemic chemotherapy combined with HAART since they usually presented at advanced stage of disease. Hence, treatment decisions for AIDS-related malignancies are guided largely by the presence and extent of symptomatic disease. Anaemia was a common finding and this is usually due to the chronic disease but rarely due to haemolysis secondary to high fever. Standard chemotherapy for cancer patients which is intensive may not be appropriate in the HIV setting as these patients often have decreased immune status which is further worsened by high risk of infectious complications.

Treatment related toxicities especially haematological complications were also substantial. Inadequate supportive care, occasional lack of cytotoxic drugs and absence of modern facilities for therapy combined to make the disease outcome worse than expected. Even with the immune restoration afforded by HAART, low-dose chemotherapy was safely administered to some of the patients because of the myelosuppressive effects of cytotoxic drugs, which might have caused further immune suppression. This implies that one may not get the desired cytoreduction of the tumour-hence the challenges involved. Although optimal treatment of these neoplasms is at present uncertain, recent advances in chemotherapy, ARV drugs and supportive care protocols are allowing for more aggressive management of many AIDS-related cancers.Improved outcome with combination chemotherapy have been reported in the highly active antiretroviral therapy (HAART) era but results are still inferior compared to those HIV seronegative patients with lymphoid malignancies.[21] All the HIV seropositive patients received HAART regimen combination of Stavudine 40mg bid, Lamivudine 150mg bid and Nevirapine 200mg daily for 2weeks and then bid.

In conclusion, the seroprevalence of HIV infection in patients with lymphoid malignancies was 4.12%. Of the 11 HIV seropositive lymphoid malignant patients, NHL was the most common neoplasm associated with HIV infection in Black race in concordance with studies in the Diaspora.

REFERENCES

1. **Cheung MC, Pantanowitz L, Dezube BJ.** AIDS-related malignancies:emerging challenges in the era of highly active antiretroviral therapy. Oncologist 2000;10(6):412-26.

2. **Reynolds P, Saunders LD, Layefsky ME, Lemp GF.** The spectrum of acquired immuno deficiency syndrome (AIDS)-associated malignancies in San Francisco, 1980-1987. Am J Epidemiol 1993; 137(1): 19-30.

3. **Bain BJ.** Lymphomas and reactive lymphoid lesions in HIV infection. Blood Rev 1998; 12(3): 154-62.

4. **Tossing G.** Immunodeficiency and its relation to lymphoid and other malignancies. Ann Hematol 1996; 73(4): 163-7.

5. The Non-Hodgkin lymphoma Pathologic Classification Group. National Cancer Institute Sponsored Study of classification of non-hodgkin lymphomas: summary and description of a Working Formulation for clinical usage. Cancer 1982; 49: 2112-2135.

6. **Blattner WA.** Human retroviruses: their role in cancer. Proc Assoc Am Physicians 1999; 111(6): 563-72.

7. **Feigal EG.** AIDS-associated malignancies: research perspectives. Biochim Biophys Acta 1999; 1423(1): C1-9.

8. **Franceschi S, Dai Maso L, La Vecchia C**. Advances in the epidemiology of HIV-associated non-hodgkin's lymphoma and other lymphoid neoplasms. Int J Cancer 1999; 83(4): 481-5.

9. **Chiu BC, Weisenburger DD.** An update of the epidemiology of non-hodgkin's lymphoma. Clinical lymphoma 2003; 4: 161-68.

10. **Ferris TJ, Garcia CJ, Berbel TO, Clar GS.** Risk factors for non hodgkin's lymphoma. Anales Espandes de Pediatria 2001; 55: 230-38.

11. **Sanpakit K, Veerakul G, Kriengsuntornkij W, Chokephaibulkit K, Tanphaichitr VS, Mahasandana C.** Malignancies in HIV-infected children at Siriraj hospital. J Med Assoc Thai 2002; 85 Suppl 2:S542-8.

12. **Ocheni S, Aken'ova YI.** Association between HIV/AIDS and malignancies in a Nigerian tertiary institution. West Afr J Med 2004; 23(2): 151-5.

13. **Analo HI, Akanmu AS, Akinsete I, Njoku OS, Okanny CC.** Seroprevalence study of HTLV-1 and HIV infection in blood donors and patients with lymphoid malignancies in Lagos, Nigeria. Cent Afr J Med 1998; 44(5): 130-4.

14. **Mosthaf FA, Hanhoff NJ, Goetzenich A, Wolf E, Knechten H.** High incidence of non-AIDS-defined cancers among HIV-infected patients in Germany. Dtsch Med Wochenschr 2006; 131(34-35): 1849-52.

15. **Ravandi F, Verma A, Ridgeway J, Pursell K**. Chronic lymphocytic leukaemia (B-CLL) occurring with human immunodeficiency virus (HIV) infection: implications. Leuk Res 2003; 27(9): 853-7.

16. **Rubio R.** Hodgkin's disease associated with human immunodeficiency virus infection. A clinical study of 46 cases. Cooperative Study Group of malignancies Associated with HIV infection of Madrid. Cancer 1994; 73(9): 2400-7.

17. **Rabkin CS.** Association of non-AIDS-defining cancers with HIV infection. J Natl Cancer Inst Monogr 1998; 23: 23-25.

18. **Lozano-Molero M, Ribera JM, Nomdedeu B, Llebaria C, Campo S, Montserrat E, et al.** Malignant lymphomas (non-hodgkin's lymphoma and hodgkin's disease) associated with infection by the human immunodeficiency virus. Study of 9 cases. Med Clin (Barc) 1989; 92(8): 302-5.

19. **Olivera M, Teira R, Munoz J, Olabarria I, Zubero Z, Cisterna R, et al.** Incidence of lymphoid neoplasms in patients with HIV infection. Enferm Infecc Microbiol Clin 1994; 12(2): 86-9.

20. **Omoti CE, Halim NKD.** Adult lymphomas in Edo state, Niger Delta region of Nigeria-clinicopathological profile of 205 cases. Clin Lab Haem 2005; 27:302-306.

21. **Cheung MC, Pantanowitz L, Dezube BJ.** AIDS-related malignancies: emerging challenges in the era of highly active antiretroviral therapy. Oncologist 2005;10(6):412-26.