

## AIDS-Related Lymphomas in Nigeria

R.A. Bolarinwa, M.A. Ndakotsu, A.A. Oyekunle, L. Salawu, N.O. Akinola and M.A. Durosinmi

*Department of Haematology and Immunology Obafemi Awolowo University and Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria*

Aggressive non-Hodgkin's lymphoma (NHL), including primary central nervous system (CNS) lymphoma, lymphoblastic lymphoma and non-endemic Burkitt's lymphoma have been recognized as AIDS-defining cancers in most developed countries. However, HIV/AIDS epidemics appear not to have been associated with higher incidence of lymphomas in Africa. We therefore carried out this study to highlight the significance or otherwise of HIV/AIDS epidemics in the pathogenesis of lymphomas in a population of Nigerians with the disease. Since January 1993 to the present, all patients with haematologic cancers are routinely screened (following appropriate counseling) for HIV infection. Patients with a histological diagnosis of malignant chronic lymphoproliferative diseases {non-Hodgkin lymphoma (NHL), chronic lymphocytic leukaemia (CLL), Burkitt's lymphoma (BL) and Hodgkin lymphoma (HL)} at the Obafemi Awolowo University Teaching Hospitals' Complex, Ile-Ife from January 1993 to August 2008 were noted. Those patients confirmed to be HIV/AIDS positive among the cohort with lymphomas were retrospectively studied using their clinical case notes. Data obtained were analyzed using appropriate descriptive and inferential statistics. A total of 391 patients were histologically confirmed to have lymphoma {NHL-109, (27.9%); CLL-76, (19.4%); BL-178, (45.5%) and HL-28, (7.2%)} during the study period. Nine patients (2.3%) were confirmed to be HIV- positive, all within the age bracket 24-60 (median = 50) years. Six of these, five males and one female, ages 24-60 (median = 37.5) years, had NHL while another three, all females (age 50 – 68years; median = 56 years) had CLL. None of the patients with HL and BL were HIV positive. Patients with NHL presented at advanced stage of the disease (at least clinical stage IIIb), and all those with CLL presented at stage C of the International Working Party Classification. All the HIV-positive patients with NHL succumbed to the disease within one to three weeks of admission into the hospital. The prevalence of AIDS-related lymphomas is 2.3% compared to 4.4% found in the general population. However, it is interesting that no single case of AIDS-associated BL was seen, despite the fact that Burkitt's lymphoma is endemic in this part of the world. All the patients presented at a very advanced stage of the disease with significantly shortened survival.

**Key-Words:** HIV/AIDS, lymphoma, Nigerians.

Lymphomas in human immunodeficiency virus (HIV) positive individuals are predominantly aggressive B cell diseases and are considered acquired immune deficiency syndrome (AIDS) defining and often time are the initial manifestation of AIDS [1]. The common HIV-associated lymphomas include Burkitt's lymphoma (BL); other less aggressive non-Hodgkin's Lymphomas (NHL) such as diffuse large B-cell lymphoma (DLBCL); primary effusion lymphoma (PEL), plasmablastic (lymphoblastic) lymphoma of the oral cavity and primary central nervous system lymphoma [2,3]. Since 1981 when the virus was first discovered in the United States, the incidence of lymphomas have been on the increase [4]. Before the advent of highly active antiretroviral therapy (HAART), primary central nervous system lymphoma and BL was reported to have increased 1000 fold, incidence of Hodgkin's lymphoma increased up to eight fold and NHL increased 60-200 fold [5-7]. Epidemiological studies also

confirmed the influence of HIV/AIDS on the geographic pattern of NHL and other cancers including those that were non AIDS-defining [7]. The risk for cancer was increased in both AIDS-defining and non AIDS-defining malignancies [8,9].

In most reports, NHL remains mostly affected by the HIV pandemic [7-10]; in all, AIDS-related lymphoma is an increasing cause of morbidity and mortality in regions of the world where the burden of HIV infection is greatest, such as Africa [11]. Lymphomas in HIV patients are heterogeneous with several pathogenetic mechanisms; including chronic antigen stimulation, genetic abnormalities, and cytokine dysregulation. Also, the impairment of the normal function of natural killer cells as a result of lack of helper signals from CD4+ T-lymphocytes is suggested to be a major mechanism of increased susceptibility to cancer development [12-14].

HIV-related lymphomas are monoclonal and are characterized by genetic abnormalities involving oncogenes MYC, BCL-6 and the tumour suppressor genes [2]. Epstein Barr virus (EBV) is identified in neoplastic cells of approximately 60% of patients with HIV-related lymphomas [2]. The first reported case of HIV/AIDS in Nigeria was in 1986 [15] and following the pandemic the sero-prevalence of HIV/AIDS in Nigeria has risen from 1.8% in 1991 to 4.4% in 2005 [16]. This study therefore sought to highlight the significance or

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Address for correspondence: Dr. RA Bolarinwa. Department of Haematology and Immunology, Faculty of Basic Medical Sciences, Obafemi Awolowo University, Ile-Ife, Nigeria. E-mail: bolarinwaraa@yahoo.co.uk, rbolarin@oauife.edu.ng. Phone: +234 803 711 5854.

otherwise of HIV/AIDS pandemic in a population of Nigerians with lymphomas.

### Material and Methods

Since January 1993, all patients with haematologic cancers are routinely screened (following appropriate counseling) for HIV 1 and 2 infections.

All patients with a histological diagnosis of malignant chronic lymphoproliferative diseases including NHL, CLL, BL and HL at the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife from January 1993 to August 2008 were reviewed. Information was obtained for patients that were confirmed HIV positive amongst this cohort. These include patients' biodata, histological type of the cancer and clinical staging at diagnosis, haematologic and biochemical results and therapy/treatment outcome. Data were analyzed using appropriate descriptive and inferential statistics and a  $p$ -value  $\leq 0.05$  were statistically significant.

### Results

A total of 391 patients were histologically confirmed with lymphomas: BL-178 (45.5%); NHL-109 (27.9%); CLL-76 (19.4%), and HL-28 (7.2%) during the period under review. Of these, nine patients (2.3%) were confirmed HIV positive. Their ages ranged from 24-60 (median=50) years. Table 1 shows the percentage of HIV-positive patients amongst different lymphoma sub-group. Many more patients were males (Male: Female ratio = 5:4).

Six patients, male/female = 5/1, aged 24-60 (median = 37.5) years had NHL while three, all females aged 50-68 (median = 56) years had CLL. None of the patients with HL and BL were HIV positive. All patients with NHL presented at a clinically advanced stage of the disease (at least clinical stage IIIb) and one patient (11.1%) had co-infection with pulmonary tuberculosis. All patients with CLL presented in stage C (International Working Party classification). None of these patients lived long enough to have chemotherapy or antiretroviral agents. All the patients with NHL succumbed to their disease within one to three weeks of admission into our facility.

### Discussion

The incidence of AIDS-related lymphoma in this study is 2.3%. Earlier reports shows that the burden of HIV infection parallel the increasing morbidity and mortality from AIDS related lymphomas, most especially in regions of the world where prevalence is highest [11]. This is however not the case in this study probably because it is a single centre, hospital based study. The majority of the affected patients in this series had NHL which is consistent with various other reports [2,12,15], and this further reinforced the AIDS-defining status of NHL. It is however interesting to note that there was no case of AIDS associated BL in spite of the high percentage of BL in this series and

**Table 1.** Table showing the percentage of HIV-positive patients amongst the different Lymphoma sub-group. (JAN.1993 - AUG 2008).

Lymphoma type	Total	HIV reactive (%)
NHL	109	6 (5.5%)
HL	28	0
CLL	76	3 (3.9%)
BL	178	0
Total	291	9 (2.3%)

NHL = Non Hodgkin's Lymphoma. HL = Hodgkin's Lymphoma. CLL = Chronic Lymphocytic Leukaemia. BL = Burkitt's Lymphoma.

more importantly the endemicity of BL in this part of the world and also BL being commonest cancer in Nigerian children [17]. This result is however in tandem with an earlier report by Chitsike et al. [9] from Zimbabwe. The probable explanation may be because BL is predominantly a childhood malignancy and/or as a result of yet unidentified factors.

Also, none of the patients with HL had HIV infection and this is similar to what was earlier reported from Kenya [15]. The clinical presentation of these patients characterized by advanced clinical stage and high histological grade is similar to earlier report [11]. However, the median survival of 2 weeks is abysmally low compared to a median of 7-8 months previously reported [11]. However, this should be viewed against the background of relatively high cost of chemotherapeutic agents, poverty, budding health insurance and presentation in advanced clinical stage of the disease [18].

### Conclusion

The prevalence of AIDS-related lymphomas is 2.3% in this series compared to 4.4% observed in the general population. However, it is interesting that no single case of AIDS-associated Burkitt's lymphoma was recorded despite its endemicity in this part of the world. All our patients presented at a very advanced stage of the disease with a significantly shortened survival.

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