Epidemiology, Clinical Presentation, Staging, Diagnosis and Treatment of AIDS Associated Non-Hodgkin’s Lymphoma

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Sub-Saharan Women

- Cervix uteri: 25.4%
- Breast: 17.4%
- Other: 28.6%
- Esophagus: 2.6%
- Colon and rectum: 2.9%
- Ovary, etc.: 3.8%
- Non-Hodgkin's lymphoma: 3.8%
- Kaposi's sarcoma: 6.2%

Sub-Saharan Men

- Other: 40.0%
- Liver: 13.3%
- Kaposi's sarcoma: 15.9%
- Colon and rectum: 3.8%
- Stomach: 4.5%
- Non-Hodgkin's lymphoma: 5.8%
- Esophagus: 6.0%
- Prostate: 10.6%
Non-Hodgkin’s Lymphoma NHL

- **HIV Influence**
  - NHL is significantly increased in HIV infection.
  - Subtypes of NHL are different in HIV population compared to the non-HIV population.
  - Many subtypes of NHL occur in HIV infected patients but certain subtypes are more common.
  - Other viruses such as EBV, HHV8 (KSHV) and HTLV-1 vary by geographic location and may influence the subtype of lymphoma seen.
HIV Burden in Sub-Saharan

- Nigeria with population (around 149 million) means that by the end of 2009, there were 3.3 million people living with HIV.
- South Africa has estimated 5.6 million people living with HIV and AIDS in 2009, more than in any other country.
- Kenya has an estimated 1.5 million people living with HIV; around 1.2 million children have been orphaned by AIDS; and
- Uganda has an estimated 1.2 million people living with HIV, which includes 150,000 children.
Epidemiology of AIDS Associated NHL

Malignant Lymphoma Subgroups

- The sub-Saharan Lymphoma Consortium (SSALC) examines retrospective lymphoma case tissue biopsies.
- Cases are from South Africa, East Africa (Kenya, Uganda) and West Africa (Nigeria).
- Cases are examined for morphology and immuno-phenotypes with placement into subgroups and subtypes.

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SA Western Cape HIV Negative

- primary effusion lymphoma
- Castleman's disease
- B-cell lymphoblastic lymphoma?
- mantle cell lymphoma
- T-cell lymphoblastic lymphoma?
- T-cell lymphoma
- mycosis fungoides
- marginal zone lymphoma
- plasmablastic B-cell lymphoma
- anaplastic large cell lymphoma
- small cell lymphoma
- mucosa-associated lymphoid tissue (MALT)
- Burkitt lymphoma
- other non Hodgkin's lymphoma
- follicular lymphoma
- Hodgkin's lymphoma
- diffuse large B-cell lymphoma

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Burkitt’s Lymphoma

- HIV (+) vs. HIV (-) adult BL:
  - Median age 35 vs. 19.5 yrs (p<0.001)
  - Uniformly present with B symptoms
  - Diffuse enlarged lymph nodes

- 15 weeks
INCREASE LYMPHOMA
CAPE AREA, SA

- primary effusion lymphoma
- Castleman's disease
- B-cell lymphoblastic lymphoma
- mantle cell lymphoma
- T-cell lymphoblastic lymphoma
- T-cell lymphoma
- mycosis fungoides
- marginal zone lymphoma
- peripheral T-cell lymphoma
- anaplastic large cell lymphoma
- small cell lymphoma
- mucosa-associated lymphoid tissue (MALT)
- Burkitt lymphoma
- other non-Hodgkin's lymphoma
- follicular lymphoma
- Hodgkin's lymphoma
- diffuse large B-cell lymphoma

HIV- HIV+
Nigeria Clinical Samples

- ZARIA AREA
  - ABU-Ahmadu Bello University

- ABUJA AREA
  - UCTH-Univ. of Calabar Teaching Hospital
  - IMSUTH-Imo State Univer. Teaching Hospital
  - UNTH-Univ. of Nigeria Teaching Hospital
  - UITH-Univ. of Ilorin Teaching Hospital
  - OAUTH-Obafemi Awolowo Univ. Teaching Hospital
Nigeria Clinical Samples cont...

- **ABUJA AREA**
  - UPTH-Univer. of Port-Harcourt Teaching Hospital
  - NAUTH-Nnamdi Azikiwe Univer. Teaching Hospital

See full details at: [SSALC.org](http://SSALC.org) website and [SSALC on FACEBOOK](http://SSALC on FACEBOOK)
Nigeria Epidemiology

Abuja area

B-cell lymphoma

Plasma cell lymphoma

Follicular lymphoma

Hodgkin disease

T-cell lymphomas

Burkitt lymphoma

Other

Zaria area

Burkitt lymphoma, EBV+

Burkitt lymphoma, EBV-

Hodgkin disease, EBV+

T-cell lymphomas

Diffuse large B-cell lymphoma, EBV+

Diffuse large B-cell lymphoma, EBV-

Hodgkin disease, EBV-

Other

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Castleman’s Disease/Lymphoma in KS Belt (HHV8)

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HIV-1 Clades

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Potential Genetic Influences

- Grouping of sub-Saharan population based on language.
  - Differ
  - Southern
  - Eastern
  - Western
Anti-Retroviral Treatment

ARVs

- South Africa ARV treatment role out to upward of one third of HIV infected population.
- Treatment is initiated at CD4 counts below 150
- Immune function is not recovered
- Lymphoma subtypes are those associated with immune deficiency?
ML Clinical Presentation

- The first sign of lymphoma is often a
  - painless lump or swollen gland in the neck, abdomen, underarm, or groin area.
  - Discovered during a visit to the doctor for another reason, or during a medical physical exam.

- Other symptoms may include:
  - Red patches on the skin.
  - Nausea, vomiting, or abdominal pain.
  - Coughing or breathlessness
  - Fever, weight loss.
Diagnosis
Non-Hodgkin’s Lymphoma

- Collection of cell or tissue sample
  - Aspiration cytology
  - Needle biopsy
  - Surgical excision (local)
  - Surgery with debulking removal of tissue

- Histopathology tissue sample (H&E stained)
  - Grade: low, medium, high (Working Group 1982)
  - Subgroups identified: Hodgkins, Burkitt’s,
Lymphoma Staging
Ann Arbor Staging Groups

- **Stage I**
  - Disease limited to one lymph node group or extra-nodal site.

- **Stage II**
  - Two lymph node groups or one extra nodal area + one lymph node group/same side diaphragm

- **Stage III**
  - Two lymph node groups with/without extra nodal sites above and below diaphragm.
Staging continued...

- **Stage IV**
  - Diffuse disease in one organ with distant lymph nodes.

**Other designations:**

- A - absent or no symptoms
- B - symptoms: fever, drenching night sweats, weight loss, severe itching, unusual tiredness
- X - bulky disease mass > 10cm
International Prognostic Index

- Predicts risk of re-occurrence of disease and survival
- **HIGH RISK** - 26% chance of 5 year survival
  - Age over 60 years
  - Stages III or IV
  - More than one extra nodal site
  - High LD (lactic acid dehydrogenase)
  - Poor general health, low albumin
Treatment

- **CHOP**
  - Cyclophosphamide
  - Doxorubicin (hydroxy)
  - Vincristine (Oncovin)
  - Prednisone
Treatment-Pre HAART

(A) Survival of *all* patients.

(B) Survival of pts treated with curative intent by pathologic type (pre-HAART era). BL, Burkitt’s lymphoma; DLCL, diffuse large-cell lymphoma.
Treatment - Post HAART

(A) Survival of all pts and (B) survival of pts treated with curative intent by pathologic type (HAART era). BL, Burkitt’s lymphoma; DLCL, diffuse large-cell lymphoma.

Survival by grade DLCL vs BL HAART era (> Jan 1997)
First Therapeutic Trial
HIV/AIDS Related Lymphoma
AFRICA

- Oral Therapy
  Regimen – all drugs given orally:
  - Lomustine (CCNU) – 50 mg/m² Day# 1
  - Etoposide (VP-16) – 100 mg/m² D# 1-3
  - Cyclophosphamide – 100 mg/m² D# 22-26
  - Procarbazine – 100 mg/m² D# 22-26

  Cycle repeated after 6 weeks
  Two cycles given (no CCNU C#2)

  Dose modifications made on basis of WBC, or ANC and platelet counts on days 1 and 22.
Pilot Oral Chemotherapy Protocol

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![Graph showing survival rates for high and intermediate tumor grades](image)

- **Tumor grade: High (n=29)**
- **Tumor grade: Intermediate (n=20)**

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<th>Intermediate grade</th>
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*p=0.013*
TREATMENT
AIDS-Related NHL

- Treatment for NHL has improved relatively little over the past 30 years.
- 35% durable survival can be approached with the diffuse large B cell lymphomas in HIV+ with ARV therapy and CHOP therapy.
- Other NHL may have less durable survival.
Summary

- NHL prevalence is different in South, East and West Africa
- Difference may be based on:
  - Genetic difference
  - Prevalence of EBV, KSHV (HHV8), HIV clades
  - ARV treatment criteria and availability
- Treatments cannot be designed and evaluated without specific diagnosis in ML
SSALC Collaborators

- Professors Clement Ademabowo, Institute of Human Virology, Abuja and Yawale Iliyasu, Ahmadu Bello University, Zaria, Nigeria