Lymphoma and Pathology in Sub-Saharan Africa

Current Approaches and Future Directions

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KEYWORDS

- Lymphoma • Africa • Pathology • Laboratory
- Low-income and middle-income countries

KEY POINTS

- Clinical and pathologic studies of patients not infected with human immunodeficiency virus with hematolymphoid malignancies are severely lacking in sub-Saharan Africa (SSA), but are necessary to inform and support effective treatment strategies.
- Most chemotherapeutic agents used for lymphoma treatment are inexpensive and available. As such, access to these therapies depends on accurate diagnosis and not necessarily funding.
- Targeted therapies for some lymphomas require specific diagnostic tools beyond the standard histology that is implementable in SSA.

INTRODUCTION

Cancer is a major cause of morbidity and mortality in developing countries where health systems are poorly equipped to deal with this challenge.[1] In the sub-Saharan region of Africa, the incidence of hematolymphoid malignancies is escalating in large part because of the human immunodeficiency virus (HIV) epidemic as well as population growth and aging.[2] Despite the increasing burden, infrastructure for diagnosis and treatment of hematolymphoid malignancies remains inadequate in sub-Saharan Africa

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(SSA). In high-income countries (HICs), lymphoma diagnosis and classification rely heavily on expensive ancillary tools like flow cytometry, immunohistochemistry (IHC), and cytogenetics, which are, as yet, largely unavailable in SSA and other low-income to middle-income countries (LMICs). Likewise, intensive cytotoxic chemotherapy regimens are often not tolerable in settings with limited supportive care. Despite these limitations, strategies to improve care in SSA can be devised and successfully implemented. This article describes regional lymphoma epidemiology, current local approaches to laboratory and pathologic diagnosis, and ongoing research efforts in SSA.

REGIONAL LYMPHOMA EPIDEMIOLOGY

Although limited by data quality, GLOBOCAN 2012 estimates the age-standardized rate (ASR) of non-Hodgkin lymphoma (NHL) in SSA to be approximately 3.9 per 100,000 person years, with an age-standardized mortality of 3.2 per 100,000 person years.[3] Classic Hodgkin lymphoma (CHL) further contributes to lymphoma burden with an ASR of 0.9%.[3] Even when considering only expected growth and aging of the population without increasing incidence rates, the annual number of new lymphoma cases in SSA is expected to nearly double over the next 2 decades, from approximately 25,000 in 2012 to more than 48,000 by 2035.[3]

Lymphoma epidemiology in SSA is critically influenced by the important role of infectious disease in lymphomagenesis in this region. Oncogenic herpesviruses, HIV, and holoendemic malaria all contribute to a high burden of lymphoma and a disproportionate percentage of aggressive NHL.[1,4]

Among pediatric patients, endemic Burkitt lymphoma (eBL) predominates in much of SSA, representing more than 80% of all hematologic malignancies and more than 90% of NHLs in some published cohorts.[5] eBL is almost invariably associated with Epstein-Barr virus (EBV) and follows a distribution that mirrors the malaria belt through central Africa.[1,4] Although the precise mechanistic relationship between these pathogens remains incompletely understood, prevailing models suggest that malaria infection may either inhibit EBV-specific immune responses or promote EBV lytic reactivation, in either case ultimately leading to the development of eBL.[6] Other common pediatric lymphoid malignancies in SSA include CHL, which is also generally EBV associated in this setting, and acute lymphoblastic leukemia/lymphoma (ALL).[5,7,8] Although T-cell ALL (T-ALL) accounts for approximately 15% of pediatric ALL in Western cohorts, studies have shown an increased proportion of T-ALL compared with B-cell ALL in children and adolescents of African descent in the United States (25.8% vs 14%).[9,10] Review of 58 cases of pediatric (<18 years old) ALL from Rwanda similarly reflects a higher proportion of T-ALL cases (36%) among Rwandan patients (Elizabeth Morgan, personal communication, 2017).

Among adults, lymphoma epidemiology is largely driven by the ongoing HIV epidemic in SSA. Since the early 1990s, lymphoma incidence has steadily increased throughout the region. For instance, in Kampala, Uganda, NHL ASR increased 3.0-fold and 2.3-fold in women and men, respectively, between 1991 and 2010.[11] Although this trend is not entirely attributable to HIV, the epidemic is clearly the primary driver. HIV-associated lymphomas are disproportionately aggressive B-cell malignancies, such as diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma (BL), and plasmablastic lymphoma.[7] These lymphomas are associated with high mortality in African cohorts, in which access to modern chemotherapy and supportive care is limited.[12] Although improving access to antiretroviral therapy (ART) is likely to reduce the incidence of some HIV-associated malignancies, other lymphomas, including CHL and