African Burkitt’s lymphoma: could collaboration with HIV-1 and malaria programmes reduce the high mortality rate?

Sam M Mbulaiteye, Ambrose O Talisuna, Martin D Ogwang, F Ellis McKenzie, John L Ziegler, Donald M Parkin

Burkitt’s lymphoma is an aggressive lymphoma that is common in sub-Saharan Africa but rare elsewhere.1 First described in African children by Denis Burkitt,2 the uneven distribution of Burkitt’s lymphoma attracted worldwide interest and led to seminal discoveries. For example, Epstein-Barr virus, the first virus to be associated with a human cancer, chromosomal translocations, and elucidation of molecular aberrations in MYC, Rb, and p53 genes—now regarded as central to the biology of cancer—is closely linked to Burkitt’s lymphoma.3 The striking response of this disease to chemotherapy led to more successful outcomes,4,5 and 90% of children with Burkitt’s lymphoma in developed countries are now cured successfully.6 In view of this success, we need to address why this disease remains disproportionately fatal in developing countries compared with developed countries, 50 years after cure by chemotherapy was first achieved.

African governments cannot afford curative treatments for cancer in the setting of competing priorities.6 Costs of treatment for Burkitt’s lymphoma are outranked by childhood nutritional, parasitic, and infectious diseases that are more prevalent, cause more deaths, and are cheaper to treat than is Burkitt’s lymphoma. In developed countries, the disease is treated in paediatric oncology units staffed with dedicated paediatric oncologists and oncology nurses who deliver the high-intensity, high-dose, multidrug chemotherapeutic regimens and the intensive and supportive care necessary to effectively treat the disease.7 However, Burkitt’s lymphoma was treated in Africa in the 1960s and 70s with cure rates of 50% or more reported in many studies.8-10 These results suggest that a substantial survival from Burkitt’s lymphoma is not incompatible with Africa’s meagre economic circumstances.

Investigators for the International Society of Paediatric Oncology9 reported in 2008 a 67% 1-year event-free survival among 269 children with Burkitt’s lymphoma treated in Malawi, Cameroon, and Ghana with intravenous single-agent generic cyclophosphamide and intrathecal hydrocortisone and methotrexate, for a total drug cost of US$55 per child. Similar results were reported in 2009 by the International Network for Cancer Treatment and Research in more than 300 patients treated in Tanzania, Kenya, and Nigeria. These patients were treated with three-drug regimen (intravenous cyclophosphamide, vincristine, methotrexate) and intrathecal methotrexate for a total drug cost of $250 per child. The total generic drug cost to treat 750 children with Burkitt’s lymphoma in a poor country such as Uganda—assuming a disease rate of five per 100 000 children per year12—varies from $37 500 to $187 500 (0.02-0.08% of Uganda’s health budget of $246 million).13 Nevertheless, children with Burkitt’s lymphoma—even those few who make it to the medical system—continue to die needlessly because proportionately fewer of them get life-saving drugs nowadays than they did in the 1960s and 1970s.

Data about the burden, distribution, and high mortality rate of Burkitt’s lymphoma in Africa, as well as about availability of affordable curative treatments are sparse. Cancer registration in Africa is underdeveloped; many countries have no registries, and registries that do exist cover restricted urban areas. Burkitt’s lymphoma occurs largely in poor rural communities in which reliable disease surveillance does not exist. For example, in 1462 patients with the disease admitted to the Uganda Cancer Institute from 1994 to 2004, the outcomes for only 228 (16%) could be documented.14 In 2002, the International Agency for Research on Cancer estimated that 5700 children were diagnosed with Burkitt’s lymphoma in sub-Saharan Africa,1 although this number is probably grossly underestimated. Thus, governments and donors do not appreciate the burden of Burkitt’s lymphoma and its high case fatality rate. Only rare anecdotal reports15,16 provide insight into the bleak experience of children with the disease in Africa. Several groups have expressed concern about the plight of such children7 and the acute deficiency of paediatric oncology services in sub-Saharan Africa.17 These groups have advocated establishment of paediatric oncology units, to be funded through private sector and public sector partnerships, to improve access to cancer care—as has been successfully done some in some countries in Latin America.17 Because of its high incidence, high curability, and availability of simple curative treatments, Burkitt’s lymphoma would be a logical focal disorder and might lead to the identification of children with other curable malignant diseases.

Uptake of such recommendations has been slow in many African countries with heavy burdens of Burkitt’s lymphoma, in part because of a scarcity of qualified staff and dedicated cancer facilities, but also because most African countries operate within internationally established development and public-health priority constraints. For example, the present international public health and ethical opinion that Burkitt’s lymphoma—and indeed, any other childhood cancer—is not a major public health concern because it accounts for a small proportion of childhood morbidity or mortality18 may discourage public health officials from...
countries with high incidence of Burkitt’s lymphoma from making a discretionary response. Local initiative can be helped only by change in international discourse to be supportive of the need to develop health systems for children with curable malignant diseases—such as Burkitt’s lymphoma.

The globally coordinated efforts to strengthen health systems in Africa have been impressive, especially for treatment of *Plasmodium falciparum* malaria and HIV-1 infections. Unprecedented investment in malaria and HIV-1 interventions in Africa has encouraged setting up of international and local infrastructures that have begun to improve access to high-quality clinical and preventive care. These improvements are broad-based and include upgrades to laboratory infrastructure, disease surveillance, infection control, monitoring adherence to treatments, training and retention of key staff, and more consistent drug supply.

Cooperation, coordination, and collaboration with existing malaria and HIV-1 programmes might assist pilot efforts to provide efficient and effective treatment for Burkitt’s lymphoma in Africa. Such cooperation might reverse, to some extent, the adverse structural effects of malaria and HIV-1 programmes that drain scarce human resources from mainstream health care. It could boost correlative research through improved systematic surveillance, patient identification, and referrals for treatment. Such cooperation would be logical because *P falciparum* malaria is a presumed geographical co-factor for Burkitt’s lymphoma and, in developed countries, HIV-1 infection is associated with a 60-fold-increased risk of the disease, and Burkitt’s lymphoma is often AIDS defining.

The effect of HIV-1 on Burkitt’s lymphoma risk in Africa is controversial and most instances are HIV-1 negative. However, cooperation could prompt studies to investigate the effect of malaria and HIV-1 interventions on the risk for Burkitt’s lymphoma. In turn, these studies might provide evidence for a causal link between the disease with malaria or with HIV-1 in Africa.

The moral and political basis for the huge efforts in malaria and HIV-1 is anchored in Millennium Development Goal (MDG) 6, as laid out by the UN General Assembly Special Session in 2000, to halt and reverse the spread of HIV-1, malaria and other diseases by 2015. MDG 6 (endorsed by 189 UN member nations) does not mention Burkitt’s lymphoma, despite its association with malaria, and its status as an AIDS-defining disease, at least in developed countries. Inclusion of Burkitt’s lymphoma into MDG 6 would subsequently lead to its inclusion as a condition of interest into the Declaration of Commitment on HIV/AIDS, which stipulates both a timetable for implementation and a regular review of progress. It could also mandate the collection of the disease data by the Country Response Information System, which helps with data collection and exchange across national and international boundaries to monitor MDG targets. This change could galvanise international and local efforts to find resources to support efficient and effective treatment for Burkitt’s lymphoma and other childhood cancers in Africa.

The Global Fund for AIDS, Tuberculosis, and Malaria approved $9·2 billion (57% of total funding) for 463 grants in 40 countries in sub-Saharan Africa during 2008. None targeted Burkitt’s lymphoma. Similarly, Burkitt’s lymphoma was not targeted in the $15 billion earmarked for HIV-1/AIDS prevention and treatment programmes in 15 poor countries for 2003–08, or the $48 billion for 2008–13 by the US President’s Emergency Plan for AIDS Relief. Nor was Burkitt’s lymphoma targeted in the $1·2 billion earmarked from the US President’s Malaria Initiative for malaria programmes in 15 poor countries in Africa for 2005–10. However, this funding stream has established both a governmental and local logistical framework for malaria and HIV-1 treatment that could bring mutual benefits to a Burkitt’s lymphoma treatment programme through alliances, without detraction from the malaria and HIV-1 programme goals.

Technical skills to diagnose, register, and treat Burkitt’s lymphoma exist in international groups, such as the International Agency for Research on Cancer, International Network for Cancer Treatment and Research, International Society for Paediatric Oncology, and St Jude Children’s Hospital. Collaboration with these groups could allow for the rapid introduction of efficient and effective care for Burkitt’s lymphoma alongside established malaria and HIV-1 programmes. The African Organisation for Research and Training in Cancer, whose mission is to promote cancer awareness and improve cancer diagnosis and treatment in Africa, already has a network across the continent that could be tapped.

The present attention of wealthier nations, organisations, and foundations focused on Africa provides a brief opportunity to end the unacceptably high death rates from Burkitt’s lymphoma. Collaboration between donors and governments to integrate programmes for the care of the disease into malaria and HIV-1 programmes could provide value-added, cross-subsidised primary, preventive, and curative care for Burkitt’s lymphoma, and greatly increase the quality of life-years gained per dollar spent. Universal access to treatment for this disease in Africa is a long overdue moral imperative, and could be another milestone for nascent paediatric oncology programmes in Africa, while saving the lives of thousands of African children dying from this disease.

**Contributors**

All authors contributed to writing and editing the Viewpoint and approved the final version.

**Conflicts of interest**

We declare that we have no conflicts of interest.
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