INTRODUCTION

Africa is the second largest continent, with a population of one billion, of whom the majority (874.8 million; 2011) live in sub-Saharan Africa, where life expectancy is low (54 years) [1,2]. Infectious diseases comprise the bulk of disease burden for African children. The under-five-mortality rate (USMR), a robust indicator of child health, is at 109 per 1,000 live births [3]. The major causes of death are pneumonia, diarrhoea, malaria, and neonatal complications [1,4].

Cancer is an important non-communicable cause of death in children, and it is estimated that about 148,000 children living in low-income countries suffer from cancer, according to GLOBOCAN 2008 [5]. Cure is possible in nearly 80% of childhood cancers in the developed world and treating children with cancer is cost-effective, even in low-income countries. Bhakta et al. [6] report that the total drug cost, in Malawi, for the treatment of Burkitt’s lymphoma (BL), the most common childhood cancer in Africa, was less than US$50 per patient.

Every child should have the right to health, which includes access to cancer treatment. The major problem with regards to childhood cancer in Africa is that the incidence of the disease is largely unknown and consequently there is a lack of reliable statistical data, which could influence health policies. We undertook a literature search to investigate the status of paediatric oncology in Africa.

SEARCH STRATEGY, SELECTION CRITERIA AND DATA COLLECTION

We identified original articles published in English from 2000 to the time of writing, using PubMed, Medline and Google Scholar. The search terms used were: ‘children’; ‘child (0–18 years)’; ‘cancer’; ‘Africa’; ‘epidemiology’; ‘prevalence’; ‘treatment’ and ‘outcome’. We also conducted a manual search of references in recent key review or strategy papers and cross references to identify additional articles. The papers were analysed regarding the following factors: prevalence; epidemiology; clinical protocol use; outcome; infections; supportive care; and palliative care. Two electronic surveys were also used to document the existing paediatric oncology units (POUs) in Africa with respect to their resources and challenges in providing curative treatment, supportive and palliative care. The respondents were attendees, whose names appeared in the database of the last two SIOP Africa meetings (held in Accra, Ghana, 2010, and in Cape Town, South Africa, 2012). The first survey focused on the different aspects of curative treatment resources and the second on different aspects of supportive care: staffing (nurses, doctors and allied medical professionals); drug access; feeding; access to PICU; radiology; neurosurgery and paediatric surgery services.

PAEDIATRIC CANCER EPIDEMIOLOGY AND CANCER REGISTRIES

A general lack of data on the true cancer incidence in Africa exists, due to the lack of cancer tumour registries [7–9]. Currently, tumour registries cover 11% of the African population, although data collection is variable. Such registries cover mostly the urban areas, whereas populations in large parts of Africa are predominantly rural [7]. There is also an absence of comprehensive death registration, leading to the mortality database relying only on estimates. The proportion of childhood cancer is higher in Africa, than in the developed countries, at 4.8% of all cancers and is mainly due to the higher proportion of children of the total population [7,8].

In parts of Africa, BL is the most commonly occurring cancer, with an incidence rate estimated at 40–100 per million per year in children under 15 in equatorial Africa [10], whereas the southern and western parts of Africa have a low overall incidence of all childhood cancers [9,11]. The high incidence of BL is commonly associated with Epstein–Barr virus (EBV) and holoendemic malaria [9]. A study of 21 centres in 19 sub-Saharan African countries analysed the distribution of childhood cancer in Africa between 1985 and 2011 [11]. In Southern Africa, Kaposi sarcoma (KS) was the most common paediatric malignancy in Mozambique...
(15.8%) and the second most common in Zambia (15.6%), with 12.4% in Malawi. In eastern Africa, Uganda recorded KS as the most common tumour in children (22.0%) while two Kenyan centres reported mainly BL (25.1% and 37.1%, respectively). Epidemiology data from western Kenya confirmed non-Hodgkin lymphoma (NHL) as being the most common childhood cancer in the region [12]. In Western Africa, NHL was the most common in Ghana (53.6%), in the Ivory Coast (73.6%), and in Mali (32.7%) [11]. Nephroblastoma remains one of the most common solid tumours in Africa, exceeding 10% of all paediatric cancers in many countries (Rwanda 26.0%; Ivory Coast 14.5%; Mali 17.6%; Congo 15.5%). Sixty African countries belong to the International Association of Cancer Registries [13]. Only 17 have national registries, whereas the remainder are regional or hospital-based. These registries include both children and adults with cancer, which calls into question the veracity of the data as they pertain to childhood cancer.

The South African Children’s Cancer Study Group (SACCSG) tumour registry, established in 1987, is the only existing dedicated national paediatric tumour registry in Africa. Only a small proportion has been published [14,15]. Leukaemia is the most common childhood cancer in South Africa (25.4% of all cancers), which is similar to rates in other countries. While brain tumours and leukaemia comprise almost half of childhood cancers in developed countries, brain tumours represent 13.4% of the total cancers diagnosed in children in South Africa. When two periods of time (1987–1997 and 1997–2007) were compared, the number of brain tumours decreased by half, while epithelial tumours doubled, almost exclusively as a result of the rising incidence of Kaposi sarcoma. A cancer report from rural South Africa documented childhood cancer as comprising 2.9% of all cancers, of which cancers with a genetic predisposition (retinoblastoma and nephroblastoma) comprised 35.6% [16]. ALL is reported as being the most common cancer in North Africa, followed by brain tumours (especially astrocytoma) and neuroblastoma [17–19].

In 2010 IARC, in collaboration with Stellenbosch University, offered the first training course in Africa for the registration of childhood cancer, attended by 105 participants from 14 African countries. An African Cancer Registry Network (AFCRN) [20], was established in 2011.

DIAGNOSIS

Diagnosis can be very challenging in Africa due to its lateness, the inadequacy of diagnostic facilities, and the lack of sophisticated imaging equipment and trained staff, especially pathologists [7,21–23]. To address the problem of late diagnosis, the WHO has decided to include the early signs of childhood cancer in the Integrated Management of Childhood Illnesses (IMCI) programme to assist primary care clinicians to recognise childhood cancer, and to enable them to refer cases early to specialised treatment centres [24]. The inclusion of these childhood cancer clinical signs in the IMCI should be tested in primary care clinics to determine the impact of the amendment on early diagnosis. A study from Cameroon reported the usefulness of abdominal sonar for the diagnosis of BL for staging [25].

Naresh et al. [22] reported a highly variable pathology infrastructure in Africa with regards to both personnel and equipment. Often slides or tissue blocks are sent to pathology centres in other countries that have the requisite pathology expertise [7]. Fine-needle aspiration biopsy (FNAB) has been proven to be a useful tool in LMICs for diagnosing childhood cancer. Such biopsy has had a sensitivity of 96.5%, and a specificity of 97%, with a positive and negative predictive value of 99% and 90% respectively, with a diagnostic accuracy of 97% [26].

INFECTIONS AND CHILDHOOD CANCER IN AFRICA

According to UNICEF, 1 in every 10 children born in sub-Saharan Africa, die before their fifth birthday [27]. At least half of these deaths can be blamed on four major infections: pneumonia (18%); malaria (17%); diarrhoea (12%); and HIV/AIDS (3%). Progress has been made and between 1990 and 2012 in sub-Saharan Africa with a reduction in U5MR of 45%. Children with cancer may succumb to common and often preventable infections, which may pose an obstacle to the successful delivery of childhood cancer care. Ninety per cent of deaths from malaria occur in sub-Saharan Africa, mostly among young children. Despite impacting on case management in childhood cancer care by introducing another cause for pyrexia in myelosuppressed patients, published evidence suggests that cancer patients are no more likely to have a fatal episode than are other children [28].

Apart from their massive impact on the survival of children receiving cancer care in Africa, infections have also shaped the burden of malignant disease in very significant ways. Malaria and EBV cooperate to produce endemic BL, and the HIV/AIDS epidemic has resulted in an increase in HIV-associated malignancies, particularly KS, which was already endemic in some areas due to a high prevalence of human herpes virus 8 (HHV8) [29–31]. Endemic BL occurs in children under 15 in the ‘lymphoma belt’, which corresponds geographically with the malaria belt [10]. The ability of EBV, especially in respect of infections that occur early in life [31,32], to transform lymphocytes by inducing the translocations typically found in BL, appears to be augmented by the intensity of malarial parasitaemia [33].

While there is a paucity of evidence that the HIV/AIDS epidemic has led to a significant increase in BL in endemic areas, there has been an increase in areas where sporadic BL predominates, such as South Africa [34–36]. By contrast, there has been a massive increase in the incidence of HHV8-driven KS, with outcomes for both remaining generally poor, due to advanced presentation and multiple co-morbidities [34,37–39]. The rollout of highly active anti-retroviral therapy (HAART) is decreasing mother-to-child transmission, and improving outcomes for HIV-infected children with cancer [40,41].

The incidence rate of tuberculosis is higher in children with malignancy than it is in the general population, and was reported to be as high as 9,000 per 100,000 per year in one study that was conducted in sub-Saharan Africa [42]. Tuberculosis is a confounding co-morbidity, which may lead to diagnostic confusion, especially in HIV-infected patients, and the coincidence of tuberculosis and HIV is a potentially lethal combination, leading to poorer outcomes, and creating the potential for multiple-drug interactions [43–45]. Research into cancer-associated infection is expanding, and such issues as the incidence and antibiotic sensitivity of nosocomial infections, the effects of antibiotic resistance, the role of targeted immunisation, and the offering of appropriate infection control advice to parents of myelosuppressed children are becoming growing concerns [46–49].
CHILDHOOD CANCER TREATMENT IN AFRICA

POUs are established in South Africa, North Africa and certain African countries (Fig. 1, including countries with responses to surveys and GFAOP member countries). According to a survey conducted in Africa, 14 out of 48 countries provide some form of dedicated paediatric oncology service, with either a paediatric oncologist or paediatrician providing medical care. The POUs reported a median of 88 children as newly diagnosed patients per annum (with a range of 5–500). Four POUs reported the number of patients per annum (ppa) to be in excess of 200. POUs in Tanzania (>500 ppa) and Uganda (380 ppa) exemplify the stark contrast between high patient numbers and poor medical staffing numbers, with eight and four doctors per unit, respectively. In addition, a centre in Uganda reported nurse-patient ratios of 1:15 during the day, and 1:45 at night. With respect to allied medical professionals, there is a critical shortage of social workers, physiotherapists, and occupational therapists. Nearly half reported good capacity to treat children with cancer (49%). All the respondents indicated access to chemotherapy (although not necessarily subsidised), but the majority (66%) had no access to radiotherapy, and 26% reported having limited access to diagnostic pathology laboratories. More than half had a dedicated ward (65%), and reported the use of local tumour registries (52%).

Twinning initiatives between POUs in LMICs and a developed country introduced successful treatment programmes in Malawi, Cameroon, Mali and Senegal. Hopkins et al. [50] characterise a successful twinning programme as a programme led by the local health-care team to ensure sustainability. This local health-care team should recognise the need to offer childhood cancer treatment, should have strong medical and/or nursing leadership, have the support of both the hospital policymakers and the local community, as well as access to external funding and international expert partners. The twinning programmes often rely on non-governmental organisations (NGOs) for fund-raising for essential cancer medicines, whereas local health-care staff are trained in paediatric cancer care [51–53].

Fig. 1. Countries who provide children cancer services in Africa.

Supportive care is critical to the management of children with cancer in Africa. While improvements in supportive care have been shown to impact positively on outcomes for children with cancer in Africa [23,73], despite ongoing efforts, no single comprehensive qualitative report exists that examines the status of supportive care facilities in African POUs. The issue of supportive care has been briefly alluded to [23], and is included in publications on palliative care [73–75], BL [72], or cancer and nutrition [76].

In the survey regarding supportive care, 10 responses were received from eight countries: Cameroon, Ghana (2), Malawi, Morocco, Nigeria (2), Tanzania, South Africa, and Uganda. Only in one POU were supportive care drugs fully funded by the state. Access to penicillins, aminoglycosides, cephalosporins, and fluconazole was fairly ubiquitous. Only one unit had access to piperacillin tazobactam, six to amikacin, six to carbapenems, and two to amphotericin B. Only four units provided TB therapy and prophylaxis, whereas all others were limited by combination anti-TB medicines, preventing INH prophylaxis. All countries had access to malaria prophylaxis and treatment. Access to HAART was good in eight units, although the time from diagnosis to the commencement of HAART varied by several weeks between services, mostly due to access.

All units had access to nasogastric tube feeding, but some reported that continuous infusion was impossible, due to the expense of feeding pumps, and, in one unit, parents found it undesirable. Only one unit had ready access to total parenteral nutrition, and another reported access if the parents paid for it themselves. Artificially formulated semi-elemental feeds were only available in South Africa, having only just become available in Uganda’s private sector.

Seven units had access to 5HTA anti-emetics, with the remainder using metoclopramide and dexamethasone. Access to PICU services was non-existent or limited. Five units reported poor or no access to intravenous morphine, two had no access to oral morphine suspension, and although four units had access to slow-release morphine tablets, in two it had to be purchased privately.

Only one POU reported state-supported patient transport, while other units relied on donations for this purpose. Four units could provide accommodation for parents, and in two units parents either...
could sit at the bedside, or sleep on the floor. This shortage is consistent with GFAOP’s report that lists the challenges for their hospitals as follows: morphine availability is inconsistent or limited; the fear of side effects leads to reduced use; and hospital regulations limit access [69]. Often non-hospitalised patients have to buy their own pain medication. Furthermore, few POUs had written protocols for the management of pain-relieving procedures.

PAEDIATRIC PALLIATIVE CARE IN AFRICA

Late diagnosis of cancer is common in Africa and, very often, palliative care with pain relief is the only option [9]. Effective pain relief is problematic, due to weak health systems and regulations that limit opioid availability [75]. Paediatric palliative care (PPC) can be provided in hospitals, primary health-care facilities, and at the child’s home. On classifying countries providing PPC, according to the four Observatory on End of Life Care (OELC) levels, Knapp et al. found that the majority of African countries were level 1 (81%), 13.2% were level 2 (Egypt, Kenya, Nigeria, Malawi and Tanzania), 3.8% were level 3 (Uganda and Zimbabwe), and only one country (South Africa) was level 4 (Fig. 2) [77]. Challenges included lack of funds for basic health care and trained health-care workers, inadequate doctor-patient ratios, lack of general public or policymaker awareness, and the unavailability of morphine [78]. In addition, cultural beliefs were found to play an important role in Africa, sometimes preventing families from seeking help for a dying child [79].

A successful strategy for improving PPC was to change the legislation that allows trained nurse practitioners to prescribe morphine in rural areas, following the example of Uganda [78]. Another initiative for developing PPC in Africa is the establishment of pilot Beacon Centres in South Africa (HPCA), Uganda (Mildmay) and Tanzania (PASADA), which provide training opportunities for health professionals [80]. Training opportunities include face-to-face training, as well as a virtual PPC training programme on the Baobab website (www.baobabppc.org.za).

ESSENTIAL DRUG LIST IN AFRICA

The WHO Essential Drug List (EDL) includes essential medicines for childhood cancer and palliative care, which can also be used for adult cancers [81–83]. In a number of countries without universal health-care policies, parent organisations and NGOs assist with the provision of the essential drugs for cancer [84]. Recent publications by SIOP-PDOC provide guidelines for modified treatment protocols for the common childhood cancers, and supportive care, using affordable drugs from the WHO EDL, which can be used in LMICs [85–89].

ADVOCACY IN AFRICA

Sustainability of health-care programmes in Africa remains a challenge, especially when potential funders pose this question to NGOs fund-raising for health-care packages for specific diseases in LMICs [84]. These programmes, however, do offer small groups of children the potential for cure. Until these countries have pro-poor financing and universal health-care systems, such programmes offer training and provide models for good clinical practice, while advocating for child health [84,90].

SIOP has held biannual continental meetings in Africa since 1994, creating a network of health-care professionals involved in paediatric oncology, and has led to successful twinning programmes in Malawi and Cameroon. Together with the International Confederation of Childhood Cancer Parent Organisations (ICCCPO) and other local parent organisations, doctors and nurses have advocated for better access to care among policymakers in individual African countries.

CONCLUSIONS

Addressing the challenges in Africa will require a collaborative effort by the health-care workers and parents who are involved in the care of children with cancer and SIOP, offering networking opportunities through African meetings. A stepwise approach, as suggested by Israels et al. [23], involves integrating childhood cancer treatment with existing general paediatric health care, and the prioritisation of feasible interventions within the framework of available health-care resources. Local tumour registries to document childhood cancer prevalence will assist policymakers in budget allocation, and should be a priority in Africa. Twinning programmes have been implemented very successfully, and should be implemented in other countries, not yet treating children with cancer, to build local health-care staff capacity.

With foresight, there are also many opportunities for collaboration between SIOP members and the infectious disease community in Africa. It is clear that improving malaria control, for example might help to prevent BL [32]. Collaboration with such large infectious disease-based programmes as The Global Fund for AIDS, Tuberculosis and Malaria, and the US President’s Emergency Plan for AIDS Relief (PEPFAR), which have a broad footprint, could help to improve services for children with cancer [90]. Mbulaiteye et al. [91] suggested that one might take either a resource-focused approach, or a disease-focused approach. A resource-focused approach would harness existing clinical...
services to expand childhood cancer care [91]. A disease-focused approach targets specific diseases for study or intervention, and is exemplified by SIOP’s PODC recommendations for managing BL and KS in low-income settings [86,87].

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