Title: Two decades of childhood cancer care in Cameroon**: 2000 – 2020**

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Abbreviations Key:

Abbreviation	**Full term**
ABV	Adriamycin (doxorubicin), Bleomycin, Vincristine
AIDS	Acquired Immune Deficiency Syndrome
Bl	Burkitt lymphoma
BBH	Banso Baptist Hospital
BHM	Baptist Hospital Mutengene
CANCaRe	Collaborative African Network of clincal Care and Research for Childhood Cancer
CBCHS	Cameroon Baptist Convention Health Services
CPM	Cyclophosphamide
CPOG	Cameroon Pediatric Oncology Group
FAPOG	Francophone Africa Pediatric Oncology Group
GICC	Global Initiative for Childhood Cancer
HAART	Highly Active Antiretroviral Therapy

HIV	Human Immunodeficiency Virus
MBH	Mbingo Baptist Hospital
MDT	Multidisciplinary team
NGO	Non-Governmental Organization
RSA	Republic of South Africa
SIOP	International Society of Pediatric Oncology
T&CM	Traditional and Complementary Medicine
USD	United States Dollar
WHO	World Health Organization

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ABSTRACT

BACKGROUND

The aim of this study was to investigate the progress made with pediatric oncology care in Cameroon from 2000 to 2020.

METHOD

A literature search was conducted for published articles on childhood cancer in Cameroon and relevant documents and conference abstracts were reviewed. The articles were analysed under eight themes: covering detection, diagnosis, management and program development.

RESULTS

Forty publications were analysed. Cancer diagnosis was achieved with cytology, histology and simple imaging. Management for common and curable cancers was with use of modified treatment regimens for low- and middle- income settings. There was good collaboration between the pediatric oncology professionals nationally and international partners. Advocacy led to the support of the Ministry of Health with pediatric oncology specific priority actions in the latest national cancer control plan.

CONCLUSION

Commitment of childhood cancer specialists, non-governmental organizations, and the government can lead to successful childhood cancer management in a low-income country.

BACKGROUND

Cameroon is a central African country with a population of about 27 million, 42% of which are children below 15 years and 30% live on less than 1.95USD per day [1]. The

under 5 mortality is 73/1000 live births [2]. There is no universal health coverage. The annual per capita expenditure on health is about 58 USD of which 74% is out-of-pocket expenditure [1]. Infectious diseases, especially HIV/AIDS, malaria and tuberculosis, still constitute major causes of disease and death in Cameroon, yet there is an increase in the incidence of non-communicable disease such as cardiovascular diseases, diabetes, and cancer [3].

Childhood cancer is not yet a health care priority in Cameroon. Based on the data from the Yaounde cancer registry, an incidence rate of 25/1,000,000 children 0 – 14 years were reported [4]. Before the beginning of the 21st century, there were no treatment programs for childhood cancers in Cameroon. In 2000, the first childhood cancer treatment center was created in the nation's capital Yaounde [5]. The Stellenbosch University, South Africa pediatric oncology team started a twinning program with the Cameroon Baptist Convention Health Services (CBCHS) and the Beryl Thyer Memorial Africa Trust with the aim of providing curative treatment for Burkitt Lymphoma, the most common childhood cancer in Northwest Cameroon in 2003 [6]. The aim of this study is to investigate the progress made with pediatric oncology care in Cameroon from 2000 to 2020.

METHODOLOGY

Two dedicated childhood cancer programs provided ediatric oncology services in the Cameroon. The first program is at the Chantal Biya Foundation Mother and Child hospital in Yaounde where there is a 25-bed unit, led by a single pediatric haematologist/oncologist. The unit receives an average of 130 patients annually [7] The care team consisted of pediatricians and general practitioners, two of whom have

100 received pediatric oncology training, and nurses. Pathology services and blood product
101 support is available from the center Pasteur in Yaounde which is adjacent to the
102 hospital [5].
103 The second program is the childhood cancer program of the Cameroon Baptist
104 Convention Health Services. Initially the program started in Banso Baptist Hospital
105 (BBH), and later extended to Mbingo Baptist Hospital (MBH) in 2006, Baptist Hospital
106 Mutengene (BHM) in the Southwest in 2007 and Mboppi Baptist Hospital Douala
107 (MBHD) in the Littoral region in 2019, which was coordinated as a single program.
108 MBH served as the hub center and the other three are satellite centers under its lead.
109 This pediatric oncology twinning program admits an average of 120 new patients
110 annually. Care is led by a pediatric oncology-trained physician and surgeons, who
111 resides at the hub centre, MBH. Care across the hub centers is provided by physicians,
112 pediatricians, general practitioners, nurse practitioners and nurses with induction
113 training in pediatric oncology, with weekly multidisciplinary team (MDT) meetings
114 across all centers and monthly MDT meetings with consultants from Stellenbosch
115 University and Leeds Children's hospital. A pediatric surgeon, an ophthalmologist,
116 radiologist and pathologist were part of the MDT, based at the hub centre MBH.
117 (Figure 1)
118 We conducted a literature search for published articles on childhood cancer in
119 Cameroon on Pubmed, Medline and Google Scholar. We used the search terms 'child',
120 'cancer', 'pediatric', 'oncology', 'epidemiology', 'treatment', 'outcome', 'incidence',
121 'Burkitt lymphoma', 'retinoblastoma', 'nephroblastoma', and 'Cameroon'. We also
122 conducted a search for relevant documents, webpages and conference abstracts of
123 pediatric oncology professionals in Cameroon. The articles were analysed under the

themes: awareness, diagnosis, registration, epidemiology, treatment, outcome, advocacy, partnerships, traditional and complementary medicine, supportive care, palliative care and capacity building.

RESULTS

A total of 857 articles were found with the search terms of which 57 abstracts were selected for screening. After screening of abstracts, 11 articles were removed because of wrong patient population (5), wrong setting (8) or duplicates (4). Forty articles were included in the analyses (Figure 2). Two articles addressed awareness [7, 8], ten addressed diagnosis, registration and epidemiology [5, 7, 9–16], fourteen addressed management and outcomes [14, 17–29], five addressed supportive care [30–34], four addressed palliative care [35–38], seven addressed advocacy and partnerships [21, 27, 30, 33, 39–41] and two addressed traditional and complementary medicine [42, 43].

CHILDHOOD CANCER AWARENESS IN CAMEROON

There was a general low level of childhood cancer awareness in Cameroon, amongst the general population as well as amongst the health care professionals as proven by a study in the Northwest region. The health care professionals had little knowledge about childhood cancer types and signs, as well as where treatment childhood cancer services were located [8]. Low awareness resulted in late diagnosis of a patient as proven by the fact that the majority of patients diagnosed at the various treatment centers in the country were diagnosed with advanced disease (stages III and IV/metastatic disease) [7, 15, 24]. A median delay of 8 months from onset of disease to consultation at the pediatric oncology center was reported in Yaounde, with patients

seeking health care at a median of three other health care providers, including traditional healers, prior to reaching the pediatric oncology unit [7].

In order to improve awareness on childhood cancer in Northwest Cameroon, childhood cancer education activities were conducted in communities, using community radios and distribution of education leaflets. An education program, targeting primary health care workers and traditional healers, led to a significant increase in their knowledge on childhood cancer and ability to refer suspected cases for management, while collaboration with traditional healers was also useful in improving their knowledge and establishing referral pathways for children with cancer [8, 42].

DIAGNOSIS, REGISTRATION AND EPIDEMIOLOGY

Diagnosing childhood cancers was a major challenge, with the paucity of competent health professionals to recognize and investigate the disease. This was compounded by the near absence of pathology experts. In the Northwest region, for example, there were only two pathologists, serving a population of 1,913,278 [16]. Diagnosis of cancer was done, using fine needle aspiration, biopsy and cytology of body fluids [15, 24, 25]. Imaging was useful, but with the lack to advanced imaging facilities, ultrasound was reported to be essential in accurately staging patients with lymphoma [13]. Peripheral blood smear and bone marrow microscopy were shown to be effective in identification of hematological malignancies in Yaounde. These techniques confirmed the diagnosis of leukemia, and ruled out other conditions with similar symptoms, such as malaria and sickle cell anemia [9]. Additionally to the technical challenges, another major challenge to childhood cancer diagnosis in Cameroon was lack of capacity to

detect early warning signs of childhood cancer to refer patients to pediatric oncology units [7, 8].

There were significant cancer registration improvements in Cameroon during the period between 2000 and 2020. Statistics from the Yaounde Cancer registry from 2004 to 2006 were included in the third edition of the international incidence childhood cancers publication by the international agency for research on cancer [44]. The estimated incidence for all cancers was 25 per million children under 15 years [4]. The common childhood cancers in Yaounde were lymphomas, soft tissue sarcomas, leukemias, retinoblastomas and renal tumors. Burkitt lymphoma was the most common of the lymphomas [5, 14]. The CBCHS childhood cancer program initiated an electronic hospital-based pediatric cancer registry in 2008 at the three hospitals mentioned above. The first formal analysis of 1029 cases registered demonstrated the most frequent diagnoses were lymphomas, followed by Wilms' tumor, retinoblastoma, rhabdomyosarcoma and Kaposi sarcoma [16].

Burkitt lymphoma was the most common childhood cancer in the country [5, 11, 14, 15]. An incidence of 3.7/100,000 was reported in the Northwest region with clustering in the hot plain districts Nwa and Ndop [10, 11, 15]. The odds of developing Bl was reported to be 3.7 higher for non-sickle trait carriers in the region[45]. It was noticed that the proportion of Bl diagnoses in the Northwest region decreased over time from 2004 to 2015 with increasing number of other cancer types such as retinoblastoma and nephroblastoma. This was probably due to the increased access to specialised medical and pathology services [11, 12, 16]. There were some publications about the epidemiology of retinoblastoma and Hodgkin lymphoma with although reporting very few cases [29, 46, 47].

MANAGEMENT AND OUTCOMES OF COMMON CHILDHOOD CANCERS

The management of childhood cancer in Cameroon was both by provision of curative treatment for common and curable cancers, as well as palliative care. The protocols applied were modified treatment regimens with reduced toxicity to adapt to the available local resources for supportive care [39, 48]. Outcomes varied by disease and were usually challenged by difficult access to essential cancer medicines, late diagnosis and lack of registries [7, 17]. Results regarding survival were fragmented, but demonstrated improved survival for especially BL and nephroblastoma [14, 20, 22, 24, 25, 49, 50]. Proper follow up was essential for obtaining outcome information and the CBCHS centers kept both paper-based and electronic-based in dedicated childhood cancer registry offices at MBH, BBH and BHM. Additional follow up was conducted by outreach and using mobile phones to establish specific outcomes [22, 34].

Burkitt lymphoma

Hesseling et al. introduced a modified treatment protocol for Burkitt lymphoma in Northwest Cameroon in 2003 and reported an event-free survival of 61% for Burkitt lymphoma at above-mentioned three Baptist Hospitals, two of which were in the Northwest region[24](19). This was the first report on Bl survival specific to Cameroon. A salvage treatment was developed for relapse disease, which achieved also 36% survival for relapsed patients [23]. The Francophone Africa Pediatric Oncology Group (FAPOG) included patients from Yaounde, Cameroon and reportedthe overall BL survival was 60% [18]. Patient destitution level was reported to affect adherence to treatment for Burkitt lymphoma in the region, with decreased survival rates seen

especially amongst children of single mothers – highlighting the necessity for individualized psychosocial support to patients and families [34].

A follow up study of 87 Bl patients, who presented with paraplegia, reported that 33% were alive at a median follow up of 40 months with 24% having residual mobility, bladder control, or bowel control problems [51]. Patients should therefore be followed up long term to identify and offer rehabilitation for their residual problems. A 1.5% rate of HIV infection was reported in this population and survival was not affected by HIV status if the patients were treated with both ART and chemotherapy. ART and CPM-based therapy resulted in 37.5% long-term survival with 91% of the patients being advanced stage disease [20].

Nephroblastoma

In Yaounde, a five year overall survival of 70% was reported [25]. A recent publication from FAPOG demonstrated an overall survival of 72% for seven Francophone African sites, including Yaounde [27]. The first report regarding survival for nephroblastoma in Mbingo Baptist Hospital in Northwest Cameroon was 44% with a median follow up of 84 months (7 years) for 35 patients treated with both chemotherapy and surgery [28]. The CBCHS pediatric oncology units collaborated in the Wilms' tumor Africa Collaborative project and overall survival improved to 68.5% at end of treatment with decreased abandonment and death during treatment in eight of the pediatric oncology units across five African countries, some with access to radiotherapy [26, 52].

Other Cancers

Other common and curable cancers in Cameroon included retinoblastoma, Hodgkin's disease and Kaposi sarcoma. A twelve-month survival of 59.2% was reported for retinoblastoma with survival mostly affected by stage of disease [49]. In a cohort of 12 patients with Kaposi sarcoma in the CBCHS pediatric oncology units, 10 were alive after 40 months showing that a good medium term outcome can be obtained for children with KS with four cycles of ABV (doxorubicin, bleomycin and vincristine) and highly active antiretroviral therapy (HAART) [50]. A five year survival of 82% was reported for a cohort of 26 patients with Hodgkin's disease [29].

SUPPORTIVE CARE

With limited access to essential medicines and blood products, supportive care was generally provided following specified guidelines for low-and-middle income countries with emphasis on tumor lysis syndrome prevention, febrile neutropenia management, infection control and nutritional support [39]. In Yaounde, half of the patients were malnourished on admission [31]. The nutritional support program in the Northwest region included provision of daily portions of rice, groundnuts, eggs, milk and cash grant to parents to provide balanced diets for the children. This led to improvement in morbidity and death during treatment [32].

Given the few centers available, most childhood cancer patients must travel long distances from their homes to seek treatment in treatment centers. In the Northwest region, over 80% of families of Bl patients had a monthly income lower than 100 USD, which made follow up visits difficult, as they could not afford the transportation costs [34]. The CBCHS childhood cancer program provided transport cost support and a parent home was constructed to host patients who come from distant localities, to

facilitate completion of treatment and follow-up visits with the assistance of non-governmental organisations (NGOs)[34].

One aspect of dire need was psychosocial support. At Mbingo Baptist Hospital, a play lead/teacher was included in the multidisciplinary team to improve the quality of life of children during hospitalization or in the parent home, awaiting chemotherapy sessions. A survey of adolescents who survived childhood cancer at younger ages, found that many of them did not get a clear understanding of their diagnoses and they had residual challenges related to the physical and emotional effects of cancer. A psychosocial support project was launched in five pediatric oncology units in Cameroon which included training staff regarding psychosocial care, resilience building and an annual action plan for psychosocial support improvement (Kouya et al., 2020. Unpublished).

PALLIATIVE CARE

The concept of palliative care was relatively unknown in Cameroon, despite a major need for patients with advanced disease [38]. A dedicated children's palliative care component was added the CBCHS childhood cancer program in the Northwest region in 2013. This service employed a trained pediatric palliative care nurse to provide palliative care to all patients at the hospital and at home for patients with terminal disease, involving the families and community support systems [35]. This model of palliative care is recommended as the way forward in overcoming financial and cultural challenges to meet palliative care needs of our patients [38]. An evaluation of this program two years later demonstrated the improved quality of life for these patients [36]. There was a particular need for bereavement care as life for extended families were usually destabilized after losing a child to cancer [37].

PARTNERSHIPS AND ADVOCACY

The CBCHS childhood cancer program was the fruit of twinning between a local health care organization (CBCHS hospitals), a South African university as a South-South partnership (Stellenbosch University), a United Kingdom hospital (Leeds Children's hospital) and two non-governmental organizations, based in the United Kingdom (the Beryl Thyer Memorial Africa Trust, U.K, and World Child Cancer, UK). This brought together funding bodies, pediatric oncology experts, health care providers, patients, parents and survivors to work together in identifying health care needs of children with cancer and implementing interventions to ensure survival of children diagnosed with childhood cancer. Technical oversight was provided by the pediatric oncologists from Stellenbosch University, RSA, since 2003, and Leeds Children's hospital, since 2016, while management and monitoring was done by the CBCHS.

Cameroon pediatric oncology units participated in two major regional research groups. The Center in Yaounde was a member of the FAPOG group which conducted clinical research projects in Burkitt lymphoma, and nephroblastoma. This center was also supported by World Child Cancer UK. The centers of the CBCHS (MBH, BHM, BBH) were members of the Collaborative African Network for Cancer Care and Research, which conducted clinical research in nephroblastoma and supportive care improvement [33].

Local advocacy groups were created for pediatric oncology. The Northwest Childhood Cancer Parents' Organization in Cameroon was founded in 2010 as a patient/parent stakeholder group, which assisted with sensitization, advocacy, fundraising, and program evaluation. In May 2018, all healthcare professionals and civil associations involved in the care for children with cancer came together to form the Cameroon

Pediatric Oncology Group (CPOG), with the aim to improve access to diagnosis and treatment for all children with cancer in Cameroon. This group harnessed the local expertise to provide capacity building for nursing care, palliative care, childhood cancer awareness creation and referrals. It also led to an advocacy group for childhood cancer established nationally with formal collaboration status with the National Committee for the Fight Against Cancer and the Ministry of Health. In July 2020, the national strategic plan for the prevention and control of cancer 2020 – 2024 was launched which included specific priority actions for childhood cancer [53].

TRADITIONAL AND COMPLEMENTARY MEDICINE (T&CM)

Disease in the cultural context in Cameroon could be explained in many different ways and thus addressed by a multitude of traditional therapies. [54]. More than half of patients with Burkitt lymphoma in Northwest Cameroon consulted a traditional healer and many different diagnoses were obtained and managed in various ineffective and sometimes harmful ways [42]. In a recent survey regarding the use of T&CM amongst children with cancer in Northwest Cameroon, the rate of use was 67% with significant side effects including infections and worsening of cancer symptoms. Even after diagnosis, a few patients were seen to delay for hospital treatment due to the pursuit of some T&CM treatment [43]. It is recommended or optimal results in such context, that education and research relationships should be established between T&CM practitioners and childhood cancer medical experts with mutual respect, in view of finding best ways to support patients [55].

CAPACITY BUILDING

Staff capacity for childhood cancer care in Cameroon improved significantly over the last two decades. From initially one pediatric oncologist at the center in Yaounde in

2000, there were an additional three qualified pediatric oncologists in the country by 2010 [53]. When the treatment program of the CBCHS started in the Northwest region, adult physicians, nurse practitioners, and nurses managed the treatment with daily links to pediatric oncologists in South Africa. Staff subsequently were trained by expert pediatric oncologists from the twinning partners, notably the University of Stellenbosch and subsequently Leeds Children's Hospital on site in Cameroon. Three nurses were trained in pediatric oncology nursing abroad and one nurse was trained in children's palliative care. One physician had training in pediatric oncology, while another physician had undertaken pathology training. There was also research capacity building with two nurses and one physician obtaining Master's degrees, based on pediatric oncology research, in Public Health and one nurse (first author) undertook research towards a PhD candidate with the research focus on childhood cancer advocacy [8, 15, 16, 34, 56].

Capacity building also occurred within the framework of regional and international research groups, notably through FAPOG, the Collaborative African Network of Clinical Care and Research for Childhood Cancer (CANCaRe), and the International Society of Pediatric Oncology (SIOP) with local staff benefitting from physician fellowships, nurse training and continued education and mentorship [33, 57].

CONCLUSION

Childhood cancer should receive the necessary attention of health care policy makers in Cameroon to ensure improved survival according to the current goal of the Global Childhood Cancer Initiative (GICC) of the World Health Organization and the International society of Pediatric Oncology (WHO-SIOP) [58, 59]. A great deal of

progress was made in the last two decades, with the establishment of treatment centers, capacity building capacity for healthcare, and advocacy for access to care. The success was definitely due to the strong national and international collaborations between the various centers and international childhood cancer experts, which led to support from the National Ministry of Health in Cameroon.

A significant milestone was achieved with the inclusion of pediatric oncology specific priority actions in the national strategic plan for prevention and control of cancer [53]. With continued commitment of government, non-governmental organizations, charities, childhood cancer specialists, patient and parent groups, there should be an improved future for children with cancer in Cameroon within the context of the WHO-SIOP global initiative for childhood cancer with a target survival of 60% for common and curable childhood cancers by 2030 [58, 59].

Conflict of interest statement:

There is no conflict of interest.

Author contributions:

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Glenn Mbah Afungchwi participated in the study design, literature review, and drafted the manuscript.

Mariana Kruger conceptualized and contributed to study design, literature search and review, critically reviewed and revised the manuscript for intellectual content.

Francine Kouya contributed to literature search and manuscript writing.

Pius Tih contributed to literature search and critically reviewed and revised the manuscript for intellectual content.

Peter McCormick contributed to literature search and critically reviewed and revised the manuscript for intellectual content.Pondy-Ongotsoyi Angele-Hermine contributed to literature search critically reviewed and revised the manuscript for intellectual content.

Peter Hesseling conceptualised the study design, contributed to literature search and review, supervised data analysis, critically reviewed and revised the manuscript for important intellectual content

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LEGENDS:

Figure 1: Map of Cameroon showing location of dedicated pediatric oncology units

Figure 2: Selection of articles for review