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Review Article

An Update on the Status of the Most Prevalent Cancer Types in Western Africa and Their Management

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Abstract

Sub-Saharan countries have a very high burden of cancer and mortality, especially breast cancer, cervical cancer and those from an infectious origin. There is a severe shortage of health professionals, radiotherapy machines, high-quality oncological referral centres, poor availability of quality medicines and palliative care. We review and update the current cancer conditions, the possibilities for reducing suffering, international cooperation and the importance of a global push and fight against cancer.

Keywords: Sub-saharan africa; Health care system; Cancer needs; Health care shortages; Palliative care; Health care policy

Introduction

Sub-Saharan Africa (SSA), albeit the home to 11% of the global population, bears 24% of the disease burden with less than 1% of the world's wealth [1]. Life expectancy is low, given the fact that 60% of its population lives on less than $1 USD per day, with food insecurity, hunger and risk of malnutrition [2]. Most of the countries in Western and Central Africa are Low-Income Countries (LICs) with a per capita annual income of less than $1,025; seven SSA countries have lower-middle annual incomes: Ghana, Mauritania, Nigeria, Senegal, Cameroon, Cape Verde and Côte d'Ivoire, between $1,046 to $4,095 (LMICs). However, by 2019, no country in the region had reached upper-middle class status, defined by an annual income between $4,036 and $12,475 (UMICs) [3-5].

Cancer Diseases

LMICs have a very high burden of cancer and mortality, which is poorly documented in SSA due to the paucity of comprehensive and reliable data and the low quality of incidence data records. Cancer is on the rise worldwide; in 2018, 18 million cancer sufferers were detected and 9.6 million died from it; these numbers are projected to rise to 28.4 million by 2040, as Africa has not seen any technological progress [6]. Annually, AAS spends less than $100 per person compared to $8,000 per person in the US which, of course, greatly influences treatment. According to GLOBOCAN 2020 [7], there were 1,109,209 new cancer cases in Africa with 711,429 534,000 deaths between 2018 and 2019. This high rate of mortality is the result of late diagnoses, the lack of any healthcare infrastructure and the shortage of oncology professionals, with tumours being diagnosed at late stages at high rates hardly ever reached in developed countries [6,7]. Cancers in Africa occur more often in younger people, are earlier onset, more aggressive and with a more difficult response to treatment. Patients present at advanced stages with a poor prognosis and are, therefore, only amenable to Palliative Care (PC). Africa has the largest proportion of high-grade malignant tumours. The highest mortality rate in women is caused by breast cancer, responsible for 27.7% of total deaths, followed by cervical cancer (19.6%); in men, prostate cancer is responsible for 18.1% of total deaths, followed by liver cancer (9.7%) and colorectal cancer (6.9%). It appears that there is a link between African ancestry and the mortality rate from prostate cancer, as African men are 2.4-5 times more likely to die from prostate cancer than men of other races [8-11].

Breast Cancer

Breast cancer is the most common tumour in African women and the leading cause of death in SSA. Its incidence has increased in the last six years to 2.1 million (in 2018) but five-year survival is 46% in Uganda and only 12% in Gambia, compared to 90% in the USA [10,11]. Early detection and treatment is essential for control yet they are mostly diagnosed at late stages, are not adequately followed-up and are at higher risk of recurrence, regardless of age, weight or grade of tumour. At the time of diagnosis they are mostly node-positive with metastasis to the lungs, bones and liver, accompanied by skin changes (e.g. orange-peel skin) or axillary adenopathy (armpit lump) in advanced cancer. If there are abnormal findings, a biopsy will be performed, guided by mammography, ultrasound or MRI. The presence of malignant epithelial cells with stromal invasion is diagnostic. Mammography is key to early diagnosis and treatment, but is largely unavailable in most SSA countries [11-13]. There are about four sub-types of breast cancer [11-17]. The first two are called Luminal A or Luminal B, and are hormone-sensitive tumours that comprise about 65% of the disease. They can be treated with hormone therapies that attempt to block oestrogen or target the receptor to avoid Chemotherapy (CT). The most common types are hormone receptor-positive (i.e., Oestrogen Receptor [ER] and/or Progesterone Receptor [PR] positive).This high percentage of oestrogen receptor-positive disease may encourage the use of tamoxifen in premenopausal

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patients or an Aromatase Inhibitor (AI) in case of intolerance, even in cases where the receptor status is unknown [13,14,16]. The second sub-type are HER2-enriched tumours (human epidermal growth factor receptor 2): 10-15%,characterized by high expression of HER2 and proliferation gene clusters and low expression of the luminal basal gene clusters. These tumours are often negative for ER and Progesterone (PR). A third tumour type is HER2, ER, PR negative (triple negative) which accounts for 13-20% of the total. This is a very aggressive type of cancer for which there are up to eight expensive treatments to target the HER2 protein without harming other cells that do not have this expression. For these, Immunotherapy (IMT) may be an option. African women are less likely to have hormone receptor (ER/PR) positive, HER2 negative disease (47% versus 64%, respectively) and more likely to have ER/PR/HER2 negative disease (22% versus 11%,respectively) [12-15]. Early detection education, genomic platforms, breast screening and surgery are cost-effective measures to change the situation, but are not available in most sub-Saharan countries [9-16]. Between 65-80% of breast cancers can be cured. Metastatic cancer is the leading cause of death among women aged 35-65 years. The Global Breast Health Initiative presents some recommendations based on a strategic system of four resource levels: basic level, limited level, enhanced level and maximum level [16,17]. The basic level indicates the fundamental services that are necessary for the functioning of any cancer system (e.g. mastectomy). In early cases, local treatment with local surgery and RT is possible, while in advanced or metastatic cases, systemic oncological treatments (CT and targeted therapies) are used. Mastectomy is a widely used procedure in breast cancer, but is not always culturally accepted [11-13]. Breast-conserving surgery in Africa is rare due to the limited availability of Radiotherapy (RT) and Adjuvant Chemotherapy (ACT), as well as other resources for sentinel node assessment. The limited level includes second-tier services that must produce significant improvements in outcomes and can be achieved with limited financial resources and moderate infrastructure (e.g., Tamoxifen, as adjuvant therapy). The enhanced level includes Tier 3 services that are optional in a resource-constrained setting, but are important and should lead to highly improved outcomes and increase the number and quality of therapeutic options and patient choices (e.g. A.I.). The maximum level represents services that can be used in resource-intensive settings or those that can be recommended in cancer guidelines that do not take resource constraints into account [16]. To be useful, top-level resources always depend on the existence and functionality of all lower-level resources.

Cervical Cancer

Cervical cancer is one of the world's most preventable tumours and the leading cause of death in African women, five times more common in Africa than in the US and other advanced countries. Two-thirds of cervical cancers due to human papillomavirus (HPV) serotypes 16 and 18, which damage a woman's immune system and increase her risk for papillomavirus infections, can be prevented by essential steps such as vaccines, screening programmes, cytology, HPV testing or a combination of these [17-20]. In some regions, preventing HPV infection is not a health priority. In 2020, the WHO adopted a global strategy for eliminating cervical cancer by 2030 by reaching levels of 90% vaccination coverage, 70% screening coverage and 90% access to treatment for cervical cancer and pre-cancer, however, there are financial problems in implementing it. Performing screening and treatment at the same visit, thus eliminating the intermediate steps of colposcopy and histological sampling, is another strategy that can reduce patient non-compliance with follow-up, infrastructure needs and, thus, overall costs of cervical cancer prevention. Locally advanced cervical cancer, the most common form of cervical cancer in Africa, requires brachytherapy and hysterectomy to be cured.

Hepatocellular Carcinoma

Hepatocellular carcinoma is the third-leading cause of cancer-related death in Africa and one of the world's major health problems with increasing incidence. Risk factors for SSA include aflatoxin exposure, alcohol abuse, obesity, hepatitis B or C and smoking [9,10]. It occurs in younger individuals (average age 45 years) who develop advanced disease and severe liver dysfunction with poor quality of life. Vaccination against hepatitis B, which is present in 80% of cases of this tumour in SSA, is essential for its prevention.

Cancers of Infectious Origin

Worldwide, 2.2 million cases of cancer are attributable to an infectious cause. By continent, the percentage of cancers due to infection is: SSA 32.7%, China 26.1%, Australia and N. America 4%. In SSA, one in three cancers is considered to be of infectious origin, the four most frequent causes being: H. pylori, papilloma virus and hepatitis B and C. Infectious agents such as the microbiome, HIV prevalence, malaria, antibiotic resistance and lack of appropriate treatment may play a role in their genesis [21,22]. According to the National Cancer Institute (NIH), cervical cancer is caused by high-risk strains of Human Papillomavirus (HPV); stomach cancer by chronic infection with H. pylori (higher in developing countries); liver cancer by chronic infection with Hepatitis B Virus (HBV) and hepatitis C Virus (HCV); and bladder cancer by Schistosoma haematobium. Human Herpesvirus-8 (HHV-8) can cause Kaposi's sarcoma. BL is related to Epstein Barr and to chronic quaternary malaria infection.

Treatments

The four pillars of oncology to be met worldwide are to: 1) prevent all cancers that can be prevented; 2) treat all cancers that can be treated; 3) cure all cancers that can be cured; and 4) provide palliation when needed. Universal health coverage is the basis for preventing and managing cancer [9]. Prevention and early diagnosis are two basic pillars in the fight against the disease. It is estimated that 19% of cancers in men and 29% in women are attributable to modifiable factors. Generally speaking, the treatments in the local and locally advanced phase are local curative treatments, surgery and radiotherapy. In the advanced and metastatic phase, systemic treatments are based on CT, IMT and treatments directed against certain factors of the disease; they are not usually curative (except in liquid tumours); these treatments modify the natural history of the disease and have achieved great advances in the survival rates of metastatic disease such as melanoma, breast, prostate, etc. This division of treatment according to stage is not rigid, but the basic treatment is often complemented by another, so that in breast cancer, conservative surgery is often complemented by RT and systemic treatment such as CT and targeted therapy [11-15]. Knowledge of tumour histology and biomarkers (specific molecular alterations) is necessary, but biobanks are largely absent in these countries. For example, in breast cancer, the expression of the growth receptor on the cell surface, known as HER2, is determined, and in cases where it is overexpressed and favoring tumour development, drugs that specifically block this receptor, in the form of monoclonal antibodies, are used [9-20]. These treatments exist for many tumours. They generally control cancer progression longer, are less toxic overall and offer better prospects [19]. Personalised medicine requires that the patient presents at a stage where the disease

is not very advanced, when there is effective clinical, oncological and RT treatment, as well as palliative care. It targets tumours with biomarkers that can be tackled with targeted or à la carte treatments [20]. However, they are very expensive and have potentially severe side effects. Most cancers (Kaposi's sarcoma, cervical, breast and some types of Hodgkin's lymphoma) can be treated with targeted therapy. Finally, there are palliative treatments focused on symptom relief when the disease is not curable. In developing countries, there is a deficit that affects all the pillars of cancer and other collateral factors such as lack of accessibility, cultural factors, etc. Universal coverage for cancer care would be the only way in which LMIC patients could obtain appropriate treatment [23].

Hormonotherapy (HT) and Chemotherapy (CT)

Hormone-specific blockade of the hormone system is a cornerstone of breast cancer treatment (oestrogen and progesterone receptors) and prostate cancer treatment (antiandrogens). CT is the application of drugs, called cytotoxic drugs, that cause tumour cell death through the induction of DNA damage. It plays an important role in many cases but, as it is very expensive and not always available in poor countries, it is not useful in most cases. In some places in Africa, a course of CT costs US 110 and a session of RT costs US 85, which few people can afford. Its administration in this region is also more difficult due to the lack of experienced professionals, laboratories for analysis, transfusions and medication to control undesirable reactions [24,25]. For this reason, it is necessary to promote specific oncology centres, use less-toxic treatment protocols, provide effective anti-emetics and antibiotics for CT-related multidrug-resistant infections and safer transfusions [12,14,16].

Immunotherapy (IMT) and Targeted Therapies

In recent years, there have been two major advances in molecular biology that have transformed the treatment for oncology patients. When an abnormal mutation occurs in a cell, our immune system reacts to eliminate it and prevent it from developing into cancer. Tumour cells that acquire mutations are able to evade this immune system by establishing links with lymphocytes or T-cells to prevent them from acting, which blocks the lymphocyte. IMT works by breaking these bonds, drawing upon the army of lymphocytes to fight the blocked tumour cell. A few tumours benefit from this treatment, most notably melanoma and kidney tumours [20]. In most countries in Africa, there is a severe shortage of anti-cancer drugs and, where they are available, prices are prohibitively high; there are also counterfeits manifesting excellent tolerance to these drugs (e.g. no hair loss with CT) as no strategies are in place to ensure that antineoplastic drugs meet quality standards [24,25]. Almost all pharmaceutical companies now offer donations and special pricing of their drugs to LMICs, competing to be listed in the Access to Medicines Index which ranks them in relation to their contribution to the poorest countries. Without access to multidisciplinary treatment, including cytotoxic CT, surgery, RT and high-quality PC, cancer is a fatal disease. A future institutional solution to the persistent problem of inequity in the diffusion of medical innovations should specify obligations on state and corporate actors to facilitate the transfer of knowledge and technology [26]. Two years ago, Kenya developed a new way of approaching the problem by charging an $8 - $200 voucher for cancer treatment, investing 8% of its health budget to fighting this disease. With this new policy, health coverage has been extended and patients can go to private centres, thus resolving the issue of long waiting lists [24].

Surgery

Surgical care is an essential element in the cure of tumours. Globally, it is estimated that two billion people do not have access to surgical services [26]. Of the 15.2 million new cancer cases in 2015, approximately 80% potentially required surgery, some several times over, and the number was projected to double in years following. The decision to operate and surgical precision is crucial for cancer control. In Africa, surgery is the primary method of cure and the basis of oncology and palliation programs, as surgeons are often the first and only doctors to treat a cancer patient [27-30]. Cancer surgery is a basic human right as it increases breast cancer survival by 30-55% and aids prevention, diagnosis, cure, palliation and reconstruction. For colon cancers, surgery is the only option available because of the scarcity of adjuvant therapies and the need for symptom relief. It is essential in advanced cancers as a palliative to improve quality of life in palliative stomas for bowel obstruction, in reconstructive plastic surgery after mastectomy, in various head and neck interventions and in non-Hodgkin's lymphoma.

Radiotherapy (RT)

RT consists of the application of ionising radiation to destroy and induce the death of tumour cells. It plays an important and irreplaceable role in the treatment of cancer, both in terms of cure and palliation [31-34]. It is used to eradicate tumours in ENT, central nervous system, lung, breast, oesophageal, gastric and rectal cancers, prostate adenocarcinoma, gynaecological tumours and sarcomas. It is very useful as palliative therapy in brain and bone metastases, spinal cord compression, vena cava syndrome or painful locations, in neurinomas, meningiomas, pituitary adenoma, keloids and chronic inflammatory processes. Although RT benefits up to 50% of patients with these cancers or with pain and bone metastases, improves the prognosis of the disease and helps other therapies, only 10.8% of patients receive it. It is the most cost-effective tool in treating cancer alone, in combination with surgery or CT, with an average cost of about $1,500 per treatment. It requires expert staff, not just oncologists, but physicists and specialised technicians as well. The lack of RT facilities in poor countries is an issue that must be addressed in order to improve the care of cancer patients.

Paediatric Oncology

Every year there are 400,000 new paediatric cancer diagnoses (children between the ages of 0-19) and 80,000 - 100,000 children die from the disease. According to R. Atún et al. [35] from 2020 to 2050 there will be 13.7 million new cases of paediatric cancer worldwide and, of these, 9.3 million (84.1%) will occur in low- and middle-income countries. In some regions of Africa, 6% of all cancers are paediatric while, in developed countries, this figure is less than 1%. In LMICs, overall survival at two years of age is 10%-30%, compared to 80% in rich countries (HICs). Cancers in children account for 0.5% of all cancers in Europe yet, in SSA, it accounts for 4-6% [44]. They are less amenable to prevention than most adult cancers, but early diagnosis can improve the chances for survival and reduce mortality rates [35-38]. In SSA, cancer is often detected late in children[8] and they have very limited survival expectancy. In the US, childhood leukaemias have a cure rate of 90% while, in Africa, only 10% are expected to survive. This is a perverse global inadequacy [6]. In SSA, there are some specific cancers which are most prevalent in children: Burkitt's Lymphoma (BL), accounting for 50% of all childhood cancers in tropical regions), nephroblastoma (which, with surgical resection, has an 80% cure rate), retinoblastoma, non-Hodgkin's and

Hodgkin's lymphomas, rhabdomyosarcoma and Kaposi's sarcoma. Rapid diagnosis and treatment is vital to preserve function, e.g. in the case of retinoblastoma. BL has a higher incidence in malaria endemic regions, while Kaposi's sarcoma is associated with HIV infection, so antiretroviral treatment would also reduce its incidence [35-38]. There are a number of cost-effective interventions for children with cancers such as BL and Hodgkin's lymphoma and treatments that can be provided in simpler medical centres, though Wilms' tumour, acute lymphocytic leukaemia and intraocular retinoblastoma require more complex equipment. 70% of paediatric cancers are curable with appropriate diagnosis and treatment and most cures can be achieved with generic drugs and other treatments such as surgery and RT. Still, paediatric oncology is not well-developed in SSA, in part because of the priority given to infectious diseases, poor health infrastructures, delay in diagnosis, delay in care, initial care by traditional healers, abandonment of treatment, e.g. after remission in leukaemia, and malnutrition, which is as high as 50%-70% in some regions of the world and associated with higher levels of toxicity [39-44]. Disparities in cancer care can be reduced by developing resources - human capital and telecommunications infrastructure - that link institutions with different levels of funding and expertise. Many countries have been able to develop some paediatric cancer programs by collaborating directly or indirectly with foreign institutions through educational efforts (twinning or one-off support) via the internet or other distance learning resources [42-44]. Changes must be made to influence primary care and educate professionals, healers and the general public about cancer and a holistic approach to patients. This requires the following actions, listed in Table 1.

Palliative Care (PC)

Cancer patients have the right to live with the utmost dignity and best symptom control available, wherever they are. An important aspect of cancer treatment is the accessibility to PC, not only for controlling pain and improving the last moments of life, but with supportive care on a level equivalent to surgery, RT and CT. Patients tend to consult at advanced stages of the disease and have a poor prognosis. The control of severe pain and suffering that cannot be alleviated without medical intervention must be central to any healthcare system, and good PC must be ensured [45]. The Lancet Commission on Global Access to PC and Pain Control quantified the global burden of severe disease-related suffering (SHS) worldwide in 2018 and found that 80% of the 61 million people affected by pain were living in LMICs [45]. It is estimated that by 2060, 48 million people (47% of all global deaths) will die of SHS, and 83% of these deaths will occur in LMICs [46]. Currently, PC services are available in 24 of the 52 countries in the region, but only less than 5% of people have access to them. Making pain-controlling opioids available to terminally ill patients with cancer and other pathologies should be a priority.

Summary

In SSA countries there are many problems that hinder adequate cancer patient care and follow-up, particularly in those with an unstable political system and impoverished populations with poor access to a good healthcare system. Adequate management, considering the existing possibilities and international cooperation are essential in order to reduce human suffering.

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Table 1: Proposals for Improving Cancer Control in Africa [6,9,29,30,42,44,45].

Organise cancer control policies, plans and programs that are harmonised with strategies for non-communicable diseases and other health concerns.
Organise training programs for oncologists, surgeons and other specialists.
Improve equipment, including more imaging and pathology equipment.
Increasing case, incidence and mortality registries.
Create oncological infrastructures to diagnose and treat patients.
Support the development of management guidelines for treatable and curable cancers that consider not only efficacy and safety, but also resource availability.
Equity of access to patients is imperative, as 80% of the world's cancer patients are in LMICs yet have only 5% of global RT resources.
Dedicate funds to NGOs that help with screening, education, vaccines, diagnosis and treatment of tumours.
Improve drug quality control.
Promote stockpiles of essential drugs and basic palliative medicine.
Seek more effective treatment options, with shorter modes and doses of administration.
Recycle antineoplastic drugs.
Approve generic types of innovative medicines.
Explore telepathology and teleradiotherapy.
Promote Palliative Care.

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