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Spectrum of Pediatric Cancers in Mozambique: An Analysis of Hospital and Population-Based Data

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Abstract

The existing data provide little detail about the epidemiology of pediatric cancers in Mozambique. We aimed at characterizing the spectrum of pediatric cancers (0–14 years) diagnosed in Mozambique in two different calendar periods. Data were obtained from the Pathology Department of the Maputo Central Hospital (DP-HCM) (1999–2000 and 2009–2010), which receives virtually all samples for histopathological diagnosis in Maputo, with the exception of leukemia, and from the population-based Cancer Registry of Beira (2009–2010). In 1999–2000, the DP-HCM diagnosed 61 cancers. Burkitt lymphoma, malignant bone tumors, and rhabdomyosarcomas accounted for 24.6%, 11.5%, and 9.8% of all cases, respectively. In 2009–2010, the number of cancers increased to 150, reflecting a two- to threefold increase in the proportion of Kaposi sarcomas, non-Hodgkin lymphomas, nephroblastomas, and neuroblastomas.

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Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

In 2009–2010, the Cancer Registry of Beira registered 34 cases, corresponding to an incidence rate of 9.7/100,000 inhabitants in this age group; Kaposi sarcomas, lymphomas, retinoblastomas, and nephroblastomas accounted for 29.4%, 23.5%, 8.8%, and 8.8% of all cases, respectively. These data show that pediatric cancers account for an appreciable burden in Mozambique, probably reflecting a high frequency of HIV-associated cancers and improved access to diagnosis, and highlight the potential for improving surveillance in this low resource setting.

Keywords

child; Mozambique; neoplasms; public health surveillance

INTRODUCTION

In sub-Saharan Africa, childhood mortality rates are among the highest in the world [1]. Over two millions of deaths were estimated to have occurred only among children aged 5 years in 2010 [1], mainly caused by infectious diseases [2]. Cancer has a small contribution to the overall mortality burden in young age groups [1], though the management of pediatric oncological diseases in low resource settings poses important challenges. In addition to limited material and human resources, that compromise timely diagnoses and effective treatment, the cancer control efforts are further undermined by chronic malnutrition and comorbidities such as malaria, tuberculosis, or infection with human immunodeficiency virus (HIV) [3, 4].

HIV infection is highly prevalent in sub-Saharan Africa and HIV/Acquired Immunodeficiency Syndrome (AIDS)-associated malignancies are expected to reshape the spectrum of pediatric cancers in these settings [5, 6]. On the other hand, improvements in the access and quality of diagnosis, together with better surveillance, may contribute to a higher number of cancer cases being diagnosed, as well as changes in the relative importance of the different cancer types. Understanding the burden of cancer is essential for planning preventive strategies, as well as the provision of health care services in resource poor settings.

The incidence of cancer in Mozambique was estimated for 2012 by the GLOBO-CAN project, using regional data and data from neighboring countries [7], for the diagnostic groups defined in the International Classification of Diseases, 10th edition, for neoplasms. However, this grouping system based on cancer topography was developed to describe the epidemiology of cancer among adults, and the planning of pediatric oncology services requires detailed descriptive data that account for specificities of the cancers diagnosed more frequently at younger ages. Therefore, we used local sources of hospital and population-based data to characterize the spectrum of pediatric cancers diagnosed in Mozambique in two different calendar periods (1999–2000 and 2009–2010).

MATERIALS AND METHODS

The present study reports on data from the Pathology Department of the Maputo Central Hospital (DP-HCM) (1999–2000 and 2009–2010), which includes histopathological

diagnoses among the population of Maputo, the capital city of Mozambique, as well as from the Cancer Registry of Beira (2009–2010), a population-based cancer registry covering the population of Beira, the second largest city in the country. The two cities are approximately 700 kilometers apart.

Maputo

The city of Maputo has just over one million inhabitants; the mean estimated population in the age-group 0–14 years was 411 thousand in 1999–2000 and 409 thousand in 2009–2010 [8]. Data from the 2007–2008 Post-Census Mortality Survey, a national inquiry into the causes of mortality based on detailed verbal autopsy questionnaires, showed that the two most common causes of death in the city were HIV and malaria; these accounted for nearly half of the deaths in subjects aged ≥ 5 years and approximately 40% among children below 5 years of age [9].

The Maputo Central Hospital is a 1500-bed hospital that provides the most specialized level of care in the country and is the national referral center for cancer. The DP-HCM receives virtually all the specimens from Maputo City, including tissue samples taken in public hospitals and in laboratories and in most of the private clinics, as well as from autopsies. Besides the specimens from Maputo City, the DP-HCM also receives samples from patients living in other areas within the country, either presenting themselves to the Maputo Central Hospital or referred by other health care institutions.

The DP-HCM keeps a computerized database of all biological samples received for analysis, with the corresponding patient's name, sex, and age, which are obtained from the forms used to request the analyses, as well as the topography, the anatomopathological diagnosis and diagnostic method used (histology, cytology, or autopsy); no further information is routinely collected since the requests for analysis usually provide scant data on other patient's characteristics. The records of the DP-HCM do not include cancers with clinical diagnosis only or leukaemias; the latter are routinely diagnosed by the Department of Clinical Pathology and Hematology of the same hospital. We analyzed cases diagnosed at the DP-HCM among children (age < 14 years) for two calendar periods separated by a 10-year interval (1999–2000 and 2009–2010).

Beira

The city of Beira is the capital of the province of Sofala. It has approximately 450 thousand inhabitants; the mean estimated population in the age-group 0–14 years was 176 thousand in 2009–2010 [10]. In the province of Sofala, in 2007–2008, HIV and malaria accounted for just over 60% of the deaths among both children under 5 years of age and in older children [11].

The city of Beira is the catchment area of the Cancer Registry of Beira. This is a population-based cancer registry that relies on active search to gather information from the Central Hospital, other public health care institutions, and private clinics, as well as deaths due to oncological causes depicted in the death certificate [12], to identify incident cases of cancer among dwellers in the city of Beira. In the present study, we included the incident cancers

diagnosed among subjects aged 14 years in 2009 and 2010. Data for 1999–2000 were not available, as the Cancer Registry of Beira was set up in 2005.

Data Analysis

For the present study, each record was revised for *a posteriori* classification of the diagnosis according to the 3rd edition of the International Classification of Childhood Cancer (ICCC-3) [13]. We presented absolute and relative frequencies of the cancers diagnosed in the cities of Maputo (1999–2000 and 2009–2010) and Beira (2009–2010), as well as the incidence rates in Beira, for the ICCC-3 diagnostic groups. The population estimates for the selected years were obtained from the official projections of the National Institute of Statistics of Mozambique, which are based on data from the censuses conducted in 1997 and 2007 [10]. The median age of the patients, with the respective 25 and 75 percentiles, are shown using box-and-whisker plot for each diagnostic group.

RESULTS

In 1999–2000, the DP-HCM diagnosed 61 cancer cases among children 0–14 years of age. Most of the diagnoses were based on histology of biopsy samples and surgical specimens (67%) and cytology/fine needle aspiration cytology (FNAC) (31%), whereas less than 2% were based on clinical autopsies. In 2009–2010, the number of cancers increased to 150; more than half were based on cytology/FNAC, 29% on histology, and 14% on clinical autopsies. The number of cases registered by the Cancer Registry of Beira in 2009–2010 was 34, from which approximately two-thirds were diagnosed by histology (Figure 1).

In 1999–2000, in Maputo city, Burkitt lymphoma, malignant bone tumors, and rhabdomyosarcomas accounted for 24.6%, 11.5%, and 9.8% of the cases, respectively. From 1999–2000 to 2009–2010, there was a two- to threefold increase in the proportion of cases of Kaposi sarcoma, non-Hodgkin lymphomas (NHL), and neuroblastomas. In the city of Beira (2009–2010), 34 cancers were registered among children; Kaposi sarcomas, lymphomas, retinoblastomas, and neuroblastomas accounted for 29.4%, 23.5%, 8.8%, and 8.8% of all diagnoses, respectively (Table 1). Hepatic and bone tumors, other epithelial neoplasms and malignant melanomas, and Hodgkin lymphomas were more frequent around 10 years of age, while retinoblastomas, rhabdomyosarcomas, neuroblastomas, and neuroblastomas affected more often younger children (Figure 2). In 2009–2010, the estimated incidence rate of cancer in the city of Beira was 9.7/100,000 individuals 0–14 years of age, although no cases of leukaemia were registered in the period of analysis.

DISCUSSION

This study provides descriptive data on the spectrum of pediatric malignancies occurring in selected areas of Mozambique, based on the most comprehensive sources of cancer data in each of the two largest cities. There was a trend toward a higher frequency of cancers known to be associated with HIV infection, though those traditionally referred as being common during infancy were also among the most frequent.

Between 1999–2000 and 2009–2010, the population 0–14 years of age living in Maputo decreased slightly, and there was no meaningful variation in its age structure [8]. Therefore, the increase in the number of cases diagnosed by the DP-HCM in this period may be related to improvements in the diagnostic facilities and access of the population to health care services, including changes in referral patterns, as well as to an increase in the risk of pediatric cancers over the last decade.

On the one hand, there were changes in the routines for cancer diagnosis, namely through the possibility of collecting biopsy samples from brain tumors during surgical procedures and an increase in the use of FNAC. The latter can be conducted faster and at a lower cost than conventional histology, and when only minimal laboratory infrastructures are available for the relatively simple collection and processing procedures required [14]. It contributes to the accurate diagnosis of patients referred from other general hospitals or peripheral primary health centers, who otherwise would remain undiagnosed or only with clinical assessment. The increase in the use of FNAC is probably the main determinant of the trend toward a higher number of cases of nephroblastomas, neuroblastomas, and hepatic tumors. Also, the increase in the frequency of clinical autopsies performed to children contributed to an increased detection of NHL and CNS tumors. Although surgical treatment for brain tumors is available both in Maputo and in Beira, the more complex procedures are more often performed in the HCM and this may have contributed to under registration of these cases in Beira.

Variations in the exposure to infections known to be associated with cancer, especially HIV infection, are expected to have contributed to a higher number of cases, namely Kaposi sarcomas and lymphomas [15]. In 2009, the prevalence of infection in Mozambican children aged 0–11 years was 1.4% [16], and it was estimated that 27% of those eligible were under antiretroviral treatment [17]. Though there are no regional data on the prevalence of HIV infection among children, in Maputo City the proportion of infected subjects among those aged 15–49 years was 16.8% in 2009 [16], which is among the highest prevalences in the country, and the proportion of pregnant women that were infected has increased in the last decade [18].

Despite Burkitt lymphoma playing an important role in the burden of pediatric cancers in Mozambique, the variation in the number cases was smaller than could be expected taking into account the association with HIV infection [3]. This may reflect the decrease in the incidence of malaria in Mozambique; between 2003 and 2009, the incidence rates decreased from 134 to 94 per 10,000 children [19]. In fact, malaria plays an important role in the occurrence of the endemic form of Burkitt lymphoma, which is the predominant among Mozambican children, by acting as cofactor for immunosuppression and promotion of the proliferation of cells infected with Epstein-Barr virus (EBV) [20]. Another plausible explanation is a less important role of HIV infection for the occurrence of BL among children; a study, conducted in Uganda, aiming at evaluating the association between non-Hodgkin lymphoma and EBV, and how the risk is modified by HIV and other variables, showed that most of the childhood lymphomas were EBV-positive Burkitt lymphomas, with no association with HIV [21].

The number of children 0–14 years of age living in Maputo City is approximately 2.3-fold the estimated for the city of Beira, whereas the overall number of cases was more than five times higher. Since the prevalence of HIV infection is similar in these two settings (15–49 years: Maputo City, 16.8%; Sofala, 15.5%) [16], and the incidence of malaria or exposure to other environmental risk factors is not expected to be higher in Maputo, the differences in the number of patients diagnosed are more likely to reflect differences in the access to health care and health literacy, as well as in the completeness of registration. Notwithstanding, direct comparisons between the two settings should be made with caution because the data from Maputo do not come from a population based cancer registry.

The considerably lower number of lymphomas, CNS, and renal tumors in the city of Beira is likely to be explained by a lower access to FNAC and less frequent use of more complex surgical procedures and clinical autopsy in Beira, while no such limitations apply to cancers easier to diagnose, such as Kaposi sarcoma. Although we cannot rule out the contribution of subdiagnosis for the under ascertainment of leukaemia cases in Beira, the fact that no cases of were registered shows the need to improve completeness, and does not necessarily reflect a lower risk in this population. The Cancer Registry of Beira is a recent cancer registry, which is still improving the data collection procedures, and this may contribute to the under registration of several cancers; estimates from Beira are most likely lower bound estimates of the cancer incidence in the region.

In Figure 3, we compared the incidence estimates reported in this study for Beira with those reported on the vol. II of the International Incidence of Childhood Cancer [22] for other sub-Saharan countries. The incidence of leukaemias, CNS tumors, and neuroblastomas is outstandingly higher in Europe and in the SEER contributing areas, compared to the sub-Saharan settings, which is likely to be explained by a higher availability of specialized methods to diagnose these tumors. In contrast, the incidence of lymphomas and sarcomas is higher in the sub-Saharan countries, probably reflecting the high frequency of HIV infection and malaria in the latter settings. Notwithstanding, these data should be interpreted with caution due to the different calendar period being assessed as well as due to different quality and completeness of the data sources.

In Maputo, the most common diagnoses were lymphomas and sarcomas. This is similar to what was reported in Zambia [23], using data from histopathological records of the University Teaching Hospital, which was the national referral center, where 32.5% and 19% of all cases diagnosed in 1990–1992 were lymphomas and Kaposi sarcomas, respectively. Similarly, lymphomas accounted for more than half of the diagnosis in Blantyre, Malawi, during 1991 and 1998 [24]. Data from the Harare Cancer Registry for 1993–1995, in Zimbabwe, showed that leukaemia, Wilms tumor, and retinoblastoma accounted for 15.1%, 14.4%, and 11.0% of the diagnoses, respectively, and that Kaposi sarcoma and lymphomas accounted for 10.3% and 8.2% of the diagnoses, respectively [25]. The specificities of data quality in each setting make difficult to ascertain whether these differences are real or introduced by data-quality problems.

It is also interesting to compare the cancers diagnosed in Maputo in the most recent years with those registered between 1956 and 1961 [26]. During 1956–1961, only 13 cases were

registered among children aged less than 10 years (four eye, three NHL, one liver, one leukemia, one skin nonmelanoma, one kidney, one brain, and one unspecified) [26]. In the age-group 10–19 years, 56 of the 81 cases were liver cancers [26]. The much smaller number of liver cancer cases in our sample ($n = 6$ in 2009–2010) is likely to reflect a decrease in the exposure to aflatoxins [27], probably due to the improvement of the storage conditions of grains and nuts, and storage for shorter periods, as well as vaccination against hepatitis B, which was introduced in 2001 and a population coverage of 75% was reached after 2002 [28].

The interpretation of the data presented in this report is limited by the small number of cases, especially in Beira, and the heterogeneity in the completeness of registration across time periods and settings. It should be considered that the National Health System supports the cost of diagnosis and treatments in Mozambique (there are only small fees for ambulatory treatments), and therefore the lack of access to diagnostic facilities due to financial constraints of the population does not represent a major limitation of our data. However, the expenses in the private sector are fully supported by the patients, and when the treatment is not available within the National Health System (e.g., radiotherapy), only the civil servants are entitled to reimbursement of 80% of the expenses with treatment, usually conducted in South Africa or Portugal. Some patients receive treatment abroad, but this is only affordable by a small proportion of the population and even in those cases the diagnosis is most likely performed in Mozambique.

Although it is possible that populations living near the borders seek health care in nearby sanitary units in the neighboring countries, this seems unlikely to have affect our estimates meaningfully, since both Maputo and Beira are relatively far from the borders, nearly 80 and 250 kilometers from the closest border, respectively. For the cases registered in the DP-HCM, it was often impossible to distinguish the place of residence of cases presenting directly to the HCM or referred from neighboring hospitals or health centers; this results in a proportion of cases from other regions that we cannot estimate accurately, and therefore we opted for not computing incidence rates for Maputo City. For example, the total number of children with renal tumors, which are often detected when it is possible to observe and/or palpate the lump, may include patients referred to the national referral center or brought by their families, especially coming from the neighboring provinces. The same may apply to Kaposi sarcomas, despite the cases with clinical diagnosis only were not registered by our source of data in Maputo.

Since Maputo has a much higher number of inhabitants than Beira, we opted for presenting both the number of cases and the corresponding proportion in each setting and period. However, it should be taken into account that the interpretation of the trends in the proportional weight of each cancer depends on the variation in the remaining. For example, the availability of FNAC may have contributed to an increasing number of renal tumors that would otherwise remain unidentified, and the HIV/AIDS epidemic resulted in an increasing number of several HIV-associated cancers, which has contributed to a lower proportional weight of other cancers even if their trends were stable. Despite the limitations described, data on the distribution of the cancers registered in this setting are valuable information for a better understanding of the burden of pediatric cancers in Mozambique.

CONCLUSION

Our results show that pediatric cancers are responsible for an appreciable burden in Mozambique, probably reflecting a high frequency of malignancies known to be associated with HIV infection and improved access to diagnosis, while highlighting the potential for improvement in cancer surveillance in this low resource setting.

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FIGURE 1.

Proportion of cancer cases other than leukaemia, diagnosed by histology, cytology/fine needle aspiration cytology and autopsy in Maputo (1999–2000 and 2009–2010) and Beira (2009–2010). FNAC = Fine needle aspiration cytology; *Data from the Department of Pathology of the Maputo Central Hospital; †Data from the Cancer Registry of Beira.

FIGURE 2.

Age distribution of the cancer cases other than leukaemia, diagnosed in Maputo ($n = 234$; a total of 11 children diagnosed in Maputo are not represented because their exact age was not available), in 1999–2000 and 2009–2010, and Beira, in 2009–2010, by group/subcategory of the International Classification of Childhood Cancer, 3rd edition (ICCC-3).

CNS = Central nervous system; results for specific subcategories were presented only when the overall number of cases (considering the two periods and two settings being analyzed) was at least 5.

FIGURE 3.

Comparison of the crude incidence of cancer in Beira with those reported by the International Incidence of Childhood Cancer, vol. II., for two high-income areas and six sub-Saharan African settings, for all cancers (panel A) and group/subcategory of the International Classification of Childhood Cancer—ICCC (panels B to L). *Age standardized incidence rates (World standard population).

Note: The diagnostic groups of the International Incidence of Childhood Cancer, vol. II., are based on the 1st edition of the ICCC, whereas the estimates reported for Beira pertain to the 3rd edition of the ICCC. The incidence estimates were obtained for the following years: Mozambique, Beira: 2009–2010; Mali: 1987–1995; Malawi: 1991–1995; Namibia: 1983–1992; Nigeria: 1985–1992; Uganda: 1992–1995; Zimbabwe: 1990–1994; ACCIS project: 1988–1997; United States, SEER: 1983–1992.

Abbreviations: MOZ, Mozambique; MLI, Mali; MWL, Malawi; NAM, Namibia; NGA, Nigeria; UGA, Uganda; ZWE, Zimbabwe; EUR, Europe; ACCIS, Automated Childhood Cancer Information System; US, United States; SEER (B), Surveillance, Epidemiology, and End Results Program, results for black population; SEER (W), Surveillance, Epidemiology, and End Results Program, results for white population.

TABLE 1
Cancers Diagnosed Among Subjects Aged 0–14 Years in the Cities of Maputo (1999–2000 and 2009–2010) and Beira (2009–2010)

ICCC-3 diagnostic group ^d	Maputo		Beira	
	1999–2000	2009–2010	2009–2010	
	N (%)	N (%)	N (%)	IR/(10 ⁵)
(I) Leukaemias, myeloproliferative diseases, and myelodysplastic diseases	NA	NA	0(0.0)	0.0
(II) Lymphomas and reticuloendothelial neoplasms				
(a) Hodgkin lymphomas	4(6.6)	7(3.9)	3(8.8)	0.9
(b) Non-Hodgkin lymphomas (except Burkitt lymphoma)	3(4.9)	20(11.2)	0(0.0)	0.0
(c) Burkitt lymphoma	15(24.6)	18(11.0)	2(5.9)	0.6
(e) Unspecified lymphomas	2(3.3)	2(1.1)	3(8.8)	0.9
(III) CNS and miscellaneous intracranial and intraspinal neoplasms	1(1.6)	7(3.9)	0(0.0)	0.0
(IV) Neuroblastoma and other peripheral nervous cell tumors	1(1.6)	5(2.8)	1(2.9)	0.3
(V) Retinoblastoma	3(4.9)	2(1.1)	3(8.8)	0.9
(VI) Renal tumors ^b	4(6.6)	25(14.0)	3(8.8)	0.9
(VII) Hepatic tumors ^c	2(3.3)	6(3.4)	1(2.9)	0.3
(VIII) Malignant bone tumors	7(11.5)	4(2.2)	1(2.9)	0.3
(IX) Soft tissue and other extraosseous sarcomas				
(a) Rhabdomyosarcomas	6(9.8)	5(2.8)	1(2.9)	0.3
(c) Kaposi sarcoma	3(4.9)	23(12.8)	10(29.4)	2.8
(b, d, e) Other ^d	1(1.6)	14(7.8)	1(2.9)	0.3
(X) Germ cell tumors, trophoblastic tumors, and neoplasms of gonads	2(3.3)	5(2.8)	0(0.0)	0.0
(XI) Other malignant epithelial neoplasms and malignant melanomas ^e	0(0.0)	3(1.7)	3(8.8)	0.9
(XII) Other and unspecified malignant neoplasms	7(11.5)	4(2.2)	2(5.9)	0.6
All cancers, except non-melanoma skin cancer	61(100.0) ^f	150(100.0) ^f	34(100.0)	9.7

Note. ICCC-3 = International Classification of Childhood Cancer, 3rd edition.

IR = Incidence rate.

NA = Not available, which are routinely diagnosed by another department of the Maputo central hospital.

CNS = Central nervous system.

- ^aResults for specific subcategories were presented only when the overall number of cases(considering the two periods and two settings being analyzed) was at least 5.
- ^bAll were nephroblastomas, except one renal carcinoma diagnosed in Beira.
- ^cAll were hepatic carcinomas, except two cases of hepatoblastoma diagnosed in Maputo(2009–2010).
- ^dIncludes cases from the following three subcategories: fibrosarcomas, peripheral nerve sheath tumors, and other fibrous neoplasms ($n = 1$); other specified soft tissue sarcomas ($n = 4$); unspecified soft tissue sarcomas ($n = 11$).
- ^eIncludes one melanoma and five epithelial neoplasms (bladder, cervix uteri, conjunctiva, lip, and salivary gland).
- ^fDoes not include leukaemias.